Supreme Court, U.S.
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No. 01-

IN THE
**Supreme Court of the United States**

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MYLAN PHARMACEUTICALS INC.,

*Petitioner,*

v.

TOMMY G. THOMPSON, SECRETARY OF HEALTH AND HUMAN SERVICES, BERNARD A. SCHWETZ, D.V.M., PH.D., ACTING PRINCIPAL DEPUTY COMMISSIONER, U.S. FOOD AND DRUG ADMINISTRATION, and U.S. FOOD AND DRUG ADMINISTRATION,
and
BRISTOL-MYERS SQUIBB CO.

*Respondents.*

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# PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

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# PETITION FOR WRIT OF CERTIORARI

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## QUESTIONS PRESENTED

1. Whether the improper listing of a patent in the FDA's Orange Book may be asserted as a defense by an ANDA applicant in an action for infringement of the patent under 35 U.S.C. § 271(e)(2);

2. Whether, pursuant to the "well-pleaded complaint rule," an action by an ANDA applicant for declaratory judgment that a patent has been improperly listed in the FDA's Orange Book arises under the patent laws of the United States; and

3. Whether 21 U.S.C. § 337(a) precludes an ANDA applicant from bringing an action for declaratory judgment that a patent has been improperly listed in the FDA's Orange Book.

## RULE 29.6 STATEMENT

Pursuant to Supreme Court Rule 29.6, Petitioner, Mylan Pharmaceuticals Inc., declares that it is a wholly-owned subsidiary of Mylan Laboratories Inc. which has issued shares to the public.

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Mylan Pharmaceuticals Inc. (hereinafter "Mylan") respectfully petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit in this case.

## OPINIONS BELOW

The opinion of the United States Court of Appeals for the Federal Circuit is reported at 268 F.3d 1323. The order denying the petition for rehearing and for rehearing en banc is reported at 2002 U.S. App. LEXIS 2624. The decision of the United States District Court for the District of Columbia, which was reversed by the Court of Appeals, is reported at 139 F. Supp. 2d 1.

## JURISDICTION

The Court of Appeals' judgment was entered on October 12, 2001. A timely petition for rehearing and for rehearing *en banc* was denied on January 9, 2002. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

## STATUTORY PROVISIONS INVOLVED

**21 U.S.C. § 337** provides that:

(a) Except as provided in subsection (b) of this section, all such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States. Subpoenas for witnesses who are required to attend a court of the United States, in any district, may run into any other district in any proceeding under this section.

**35 U.S.C. § 271(e)** provides, in pertinent part, that:

(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import

into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit -

> (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent, or
>
> (B) an application under section 512 of such Act or under the Act of March 4, 1913 (21 U.S.C. 151-158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent,

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

**35 U.S.C. § 282** provides, in relevant part, that:

> The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:
>
> (1) Noninfringement, absence of liability for infringement or unenforceability,
>
> (2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,
>
> (3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,
>
> (4) Any other fact or act made a defense by this title.

The relevant provision of the Federal Food, Drug and Cosmetic Act, as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, codified at 21 U.S.C. § 355, is reproduced at App., *infra*, 84a.

## STATEMENT OF THE CASE

This case concerns the ability of a generic drug manufacturer to obtain relief under the Declaratory Judgment Act against the actions of a holder of a patent for a pioneer drug in listing such patent improperly with the U.S. Food and Drug Administration ("FDA"). It is Mylan's position that a challenge to the propriety of a listing of a patent in the FDA's

Orange Book[1] may, pursuant to the "well-pleaded complaint rule," be raised in a declaratory judgment action as a defense to a threatened action for infringement of the patent under 35 U.S.C. § 271(e)(2). *See Speedco, Inc. v. Estes*, 853 F.2d 909, 912 (Fed. Cir. 1988) (court looks to action declaratory judgment defendant would have brought to determine whether an action arises under the patent laws).[2] This case also involves an important issue of statutory construction concerning whether Mylan's improper-listing defense is barred by the Federal Food, Drug and Cosmetic Act. It is Mylan's position that, in holding that all private actions to enforce provisions of that Act are statutorily barred, the Federal Circuit misconstrued 21 U.S.C. § 337(a).

## A. Statutory and Regulatory Framework

The statutory scheme governing the submission and approval of applications for generic drugs (ANDAs) and the interplay between the patent and regulatory laws is contained in the Federal Food, Drug and Cosmetic Act ("FDCA"), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. No. 98-417) (the "Hatch-Waxman Amendments"), *codified at* 21 U.S.C. § 355 and 35 U.S.C. §§ 156 and 271(e). Section 505(j) of the FDCA (21 U.S.C. § 355(j)) establishes the procedures for filing and approval of abbreviated new drug applications ("ANDAs").

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[1] The FDA's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" is commonly known as the "Orange Book" because of the color of its cover. It is in the Orange Book that the FDA publishes patent information provided by NDA holders.

[2] The jurisdiction of the District Court was invoked under 28 U.S.C. § 1331, 5 U.S.C. § 551 et seq., 28 U.S.C. §§ 2201-2202 and 28 U.S.C. § 1361.

ANDAs are approved on the basis of safety and efficacy data previously submitted for the reference drug and contained in the NDA holder's approved new drug application ("NDA"). The ANDA applicant must show, *inter alia*, that its drug is bioequivalent to the reference drug. 21 U.S.C. § 355(j)(2)(A). In this case, the reference drug is BuSpar® brand of buspirone marketed by Bristol-Myers Squibb Co. ("Bristol"). Mylan (and other companies) have filed ANDAs seeking to market generic versions of this drug.

A company that has filed a New Drug Application ("NDA") must include in the NDA information about patents that claim the drug product that is the subject of the NDA. 21 U.S.C. § 355(b)(1). When, as in the present case, a patent issues after an NDA has been approved, the holder of the approved NDA is required to file with the FDA for inclusion in the Orange Book the patent number and expiration date of any patent,

> which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

21 U.S.C. § 355(c)(2). Companies that sell brand-name drugs have a considerable incentive to cause the FDA to list patents in the Orange Book. The listing of a patent is the first and necessary step that triggers a cascade of events under the Hatch-Waxman scheme that typically results in a delay of FDA approval of the generic version of the approved drug for up to thirty months. For "blockbuster" drugs, such as BuSpar®, this delay can be worth hundreds of millions of dollars to the NDA

holder. In filing the '365 patent with the FDA, Bristol attempted to create just such a delay.

With respect to listed patents that claim the approved drug or a method of using the approved drug, an ANDA applicant must include in the ANDA one of four types of patent certifications described in 21 U.S.C. § 355(j)(2)(A)(vii). Of pertinence to this case is the fourth type of certification, commonly known as a "Paragraph IV certification." If the generic drug company seeks FDA approval before the listed patent expires, it must make a Paragraph IV certification that such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted (21 U.S.C. § 355(j)(2)(A)(vii)(IV)). *See Bristol-Myers Squibb Co. v. Royce Lab.*, 69 F.3d 1130, 1131 (Fed. Cir. 1995), *cert. denied*, 516 U.S. 1067 (1996).

The timing of FDA approval of an ANDA that contains a Paragraph IV certification is determined by a statutory scheme under which the ANDA applicant must provide notice to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA refers. 21 U.S.C. § 355(j)(2)(B)(i). The Hatch-Waxman Amendments also modified the patent laws to provide that the submission of an ANDA (an application under § 505(j) of the FDCA, 21 U.S.C. § 355(j)) or a paper NDA (an application under § 505(b)(2) of the FDCA, 21 U.S.C. § 355(b)(2)) is an act of patent infringement, "if the purpose of such a submission is to obtain approval under the [FDCA] to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such a patent." 35 U.S.C. § 271(e)(2)(A); *see also Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1245 (Fed. Cir. 2000), *cert. denied*, 531 U.S. 993 (2000). This Court has explained that what is

achieved by § 271(e)(2) is "the creation of a highly artificial act of infringement that consists of submitting an ANDA or paper NDA containing the fourth type of certification that is in error as to whether commercial manufacture, use, or sale of the new drug (none of which, of course, has actually occurred), violates the relevant patent." *Eli Lilly & Co. v. Medtronic*, 496 U.S. 661, 678 (1990), *reh'g denied*, 497 U.S. 1047.

If the patent owner brings an action for patent infringement under 35 U.S.C. § 271(e)(2) against the ANDA applicant within forty-five days of receiving the ANDA applicant's notice, the FDA is precluded from approving the ANDA for a period of 30 months from the date of receipt of the notice, unless prior to that date, a court decides that the patent is invalid or not infringed, in which case approval is to be made effective on the date of the court's decision. 21 U.S.C. § 355(j)(5)(B)(iii).

**B. Factual Background**

Since 1986, Bristol has been selling in the United States an anti-anxiety medication to treat patients suffering from generalized anxiety disorder under the trademark BuSpar®. The active ingredient in BuSpar® is buspirone hydrochloride (referred to herein as "buspirone"). In 1999, Bristol's sales of its BuSpar® product exceeded $600 million.

Since Bristol began selling BuSpar® and until the time of the District Court's decision, it faced no competition from generic buspirone products. Bristol had no such competition previously, because in 1980 Bristol received a patent covering the administration of buspirone to treat anxiety disorders. By taking advantage of statutory incentives designed to encourage certain pediatric studies, Bristol was able lawfully to extend its patent exclusivity until 11:59 p.m. on November 21, 2000.

That is, beginning at 12:00 a.m. on November 22, 2000, Bristol was scheduled to face generic competition in the sale of buspirone tablets.

Mylan, a leading generic drug company, had developed a generic buspirone product and had obtained tentative FDA approval of its ANDA for that product in anticipation of the expiration of Bristol's exclusivity. Mylan expected final approval on November 22, 2000 and had product ready to ship on that day. However, just eleven hours before Bristol's exclusivity was to expire, Bristol hand-delivered to the FDA information concerning a new patent, U.S. Patent 6,150,365 ("the '365 patent"), which had issued only an hour before. Bristol requested that the FDA immediately list the '365 patent in the Orange Book.

Mylan filed suit against Bristol and the FDA in the U.S. District Court for the District of Columbia on November 30, 2000. On the same day Mylan moved for a preliminary injunction ordering that the '365 patent be delisted on grounds that the listing was improper and contrary to the statute, and, therefore, Bristol was not entitled to assert patent infringement under 35 U.S.C. § 271(e)(2) to gain the benefit of an additional 30-month stay of approval of Mylan's generic version of BuSpar®.

### C. The Proceedings Below

The District Court reviewed the '365 patent and its prosecution history and concluded that Bristol failed to meet either of the two statutory requirements under 35 U.S.C. § 355(c)(2) for listing in the Orange Book: "Mylan has shown a substantial likelihood that this court will issue a declaratory judgment stating that Bristol improperly submitted the '365

patent for listing in the Orange Book."[3] App., *infra*, 77a-78a. The District Court ordered a preliminary injunction against Bristol. App., *infra*, 78a.

Bristol appealed the District Court's decision to the U.S. Court of Appeals for the Federal Circuit. The FDA and the other federal defendants, although named as defendants in the District Court proceeding, realigned as appellees and supported Mylan's action against Bristol for delisting of the '365 patent. The Federal Circuit reviewed the judgment of the District Court and held that Mylan could not obtain relief in a declaratory judgment action against Bristol under the patent laws or the Hatch-Waxman Amendments. App., *infra*, 18a.

The Federal Circuit reversed the judgment of the District Court for two primary reasons. First, the court held that Bristol's improper Orange Book listing could not be raised in a declaratory judgment action as a defense to an admittedly threatened action for patent infringement under 35 U.S.C. § 271(e)(2). The court concluded that improper patent listing did not fall within "two broad groups" of defenses to allegations of patent infringement, namely the statutory defenses enumerated in 35 U.S.C. § 282 and equitable defenses, including unclean hands, unenforceability, inequitable conduct, misuse and laches or estoppel. App., *infra*, 15a-16a. Because Mylan's argument did not tie-in to any of these defenses, the court held that no such defense could be predicated on an improper listing under the patent laws. App., *infra*, 16a.

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[3] The U.S. District Court for the Southern District of New York, in the context of a motion to dismiss certain antitrust claims asserted by Mylan and others against Bristol, recently has also held that Bristol's listing of the '365 patent in the Orange Book was improper. *In re Buspirone Patent & Antitrust Litig.*, 185 F. Supp. 2d 363 (S.D.N.Y. 2002).

Second, the court turned to the Hatch-Waxman Amendments to consider whether they expressly permitted an "additional defense" of the nature advocated by Mylan and concluded that they do not. The Court found that no explicit statement in the Hatch-Waxman Amendments permitted an ANDA-holder to seek judicial relief. App., *infra*, 16a-17a. The Federal Circuit also found that the legislative history did not support an intent to provide any additional defenses "or to create a private action for delisting a patent from the Orange Book for a patentee's failure to comply with section 355." App., *infra*, 18a.

Concluding that Mylan had not satisfied the "well-pleaded complaint rule" by asserting a defense under the patent laws or the Hatch-Waxman Amendments, the Court determined that Mylan's declaratory judgment action was barred by 21 U.S.C. § 337(a) of the FDCA, which states that "all such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States." App., *infra*, 18a. The Federal Circuit reasoned that Mylan's declaratory judgment action rested on a violation of 35 U.S.C. § 355(c)(2) of the FDCA which sets forth the requirements for listing in the Orange Book. *Id.*

The Court subsequently denied Mylan's petition for rehearing as well as its motion to stay issuance of its mandate pending ruling on this petition. App., *infra*, 80a-83a.

## REASONS FOR GRANTING THE WRIT

Petitioner seeks review because: (1) the judgment below severely undercuts the policy behind the Hatch-Waxman Amendments by delaying the availability of generic drugs, thereby resulting in increased costs to American consumers; (2) the judgment below contravenes this Court's construction of

the Hatch-Waxman Amendments and transforms established patent law by denying an ANDA applicant the right to assert failure to state a claim as a cognizable defense to infringement under 35 U.S.C. § 271(e)(2); and (3) an important issue of federal statutory construction has been raised with respect to the effect of 21 U.S.C. § 337(a) on the right of a private litigant to seek relief under the patent laws based on a violation of the FDCA.

## I. Certiorari Should Be Granted Because the Decision Below Undercuts the Policy of the Hatch-Waxman Amendments and Will Cost the American Public Millions of Dollars in Increased Prescription Drug Costs

The Federal Circuit's decision culminates in a decided advantage to owners of patents to pioneer drugs that will have the deleterious effect of delaying entry of generic drugs for years, resulting in increased drug costs borne by the American public. This chain of events runs counter to the purpose of the Hatch-Waxman Amendments, which was to facilitate the availability of generic drugs in the marketplace.

The issue of whether improper patent listings in the Orange Book can be resolved by patent holders and generic drug manufacturers in the courts is of paramount national importance because of the escalating costs of health care in this country. Prescription drug expenditures continue to be the fastest growing component of health care.[4] The National

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[4] In 2001, total prescription drug spending rose 17.1 percent from the previous year to $154.5 billion. This trend is expected to continue with an average increase of 11.7 percent per year between 2003 and 2007, and an average increase of 10.3 percent a year between 2008 and 2011. *See* National Institute for Health Care Management Research and Educational

Institute for Health Care Management Research and Educational Foundation, *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs* 2 (Apr. 2002). The average retail price for prescription drugs has increased more than three times the rate of general inflation, thereby accounting for roughly 27 percent of the overall increase in total spending on health care. *See Id.*; The Henry J. Kaiser Family Foundation, *Prescription Drug Trends - A Chartbook Update* 8 (Nov. 2001).

The escalating costs in prescription drug spending disproportionately affects the elderly. Elderly citizens represent about 13 percent of the population, but account for almost one-third of all prescriptions dispensed in the U.S. Report of the Senate Special Committee on Aging, S. Rep. No. 105-B6 (I) at 122. The Medicare program does not cover outpatient prescription drugs sold to elderly patients, and at least 27 percent of Medicare beneficiaries (based on 1998 figures) lack any prescription drug coverage. *See* The Henry J. Kaiser Family Foundation, *Prescription Drug Trends - A Chartbook Update* 4 (Nov. 2001).

Studies have indicated that this phenomenon is also attributable to "the dominance in the marketplace of more costly brand-name drugs over less costly generic drugs." The National Institute for Health Care Management Research and Educational Foundation, *Prescription Drug Expenditures in 2000: The Upward Trend Continues* 14 (May 2001). Because

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Foundation, *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs* 3, 5 (Apr. 2002).

generic drugs cost substantially less than brand-name drugs,[5] generic drugs are a critical check against rising prescription drug expenditures. Congressional Budget Office, *How Increased Competition From Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* ix (July 1998); *see also* Merck-Medco Managed Care, L.L.C., *The Merck-Medco Drug Trend Report 2001* 6 (2001). According to the Congressional Budget Office, substituting generic for brand-name drugs has saved U.S. consumers billions of dollars. Congressional Budget Office, *supra*, at ix. Generic drug manufacturers' share of the overall market for retail prescription drugs has remained flat since 1996. The Henry J. Kaiser Family Foundation, *Prescription Drug Trends - A Chartbook Update* 10 (Nov. 2001); *see also* The National Institute for Health Care Management Research and Educational Foundation, *Prescription Drug Expenditures in 2000: The Upward Trend Continues* 14 (May 2001).

According to a number of industry reports, a significant factor in the static growth of generic drug manufacturers' share of the market is the strategy followed by brand-name drug manufacturers to extend the economic life spans of their important "blockbuster" pioneer drugs by "evergreening." "Evergreening" includes the practice of adding listings of new patents to the Orange Book to initiate patent litigation against generic drug manufacturers who have filed ANDAs (thereby invoking the automatic 30-month stay of FDA approval). *See*

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[5] According to the Generic Pharmaceutical Association, the difference in the average cost of a brand prescription drug versus a generic description drug has risen from $16.87 per prescription in 1990 to $45.96 per prescription in 2001. Because of this significant gap, the Association reports that generic drugs may constitute roughly 40 percent of all retail prescription sales but only account for 8 percent of total prescription drug spending in the U.S. Generic Pharmaceutical Ass'n., "Facts", prepared by IMS Health, available at www.genericaccess.com.

*generally* Merck-Medco Managed Care, L.L.C., *The Merck-Medco Drug Trend Report 2001* 7 (2001); Ed Hore, *Evergreening Drug Patents: A Big Issue*, THE LAWYERS WEEKLY, Feb. 2, 2001, at 12; The National Institute for Health Care Management Research and Educational Foundation, *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs* 3 (Apr. 2002).

Brand-name drug manufacturers, acting on a strong incentive to list any patents in the Orange Book remotely related to the approved drug, have effectively delayed market entry of generic drug manufacturers for years by initiating patent litigation under § 271(e)(2). *See* Aida Hollie, *Closing the FDA's Orange Book*, REGULATION, Winter 2001, at 14-17; Ed Hore, *Evergreening Drug Patents: A Big Issue*, THE LAWYERS WEEKLY, Feb. 2, 2001, at 12; Jill Wechsler, *Pressure Mounts to Revise Generic Drug Policies*, PHARMACEUTICAL TECHNOLOGY, Feb. 2001, at 16-25; 147 Cong. Rec. H3032, H3034 (daily ed. June 12, 2001) (statement of Rep. Pallone).[6]

For these reasons, the Federal Circuit's decision in this case, denying any redress by generic drug manufacturers in the courts against abuses by brand-name drug manufacturers of the patent-listing process, will have a profoundly negative economic impact. According to research reports, brand-name drug manufacturers' "evergreening" strategies have forced American consumers to incur billions of dollars in drug costs that they otherwise may not have paid. *See Recent*

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[6] The Federal Trade Commission has received several public comments supporting that improper patent listings in the Orange Book have resulted in delays of generic competition. Bureau of Competition & Policy Planning Staff, Federal Trade Commission, *Citizen Petition to the Commissioner of Food and Drug Administration*, May 16, 2001, at 2.

*Developments Which May Impact Consumer Access to, and Demand for, Pharmaceuticals: Hearing before the Subcommittee on Health of the House Committee on Energy and Commerce*, 107th Cong. 3 (June 13, 2001) (prepared statement of Bruce L. Downey, Chairman & CEO, Bar Labs., Inc. on behalf of the Generic Pharmaceutical Association) (estimated cost of Bristol's listing of the patent at issue in this case to be more than $500 million to American consumers); *see also* The National Institute for Health Care Management Research and Educational Foundation, *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs* 3 (Apr. 2002).

This concern has not gone unnoticed by the original sponsors of the Hatch-Waxman Act. Senator Hatch and Congressman Waxman, in a letter to the FDA, warned that this practice could result in unnecessary expenditures of "hundreds of millions of dollars." App., *infra*, 178a-179a.

This problem is exacerbated by the FDA's position that it will not review the merits of particular patent listings made by pioneer drug manufacturers in the Orange Book. The FDA's expertise and Congressional charter is to ensure the safety and efficacy of food and drugs. It has emphasized its lack of expertise in patent matters. The FDA's position and citation of authorities supporting such position is exemplified by its brief submitted to the Federal Circuit in this case:

> Under the [Food, Drug, and Cosmetic Act], however, FDA is not authorized to resolve disputes about the validity, accuracy, or relevancy of specific patents submitted to it. *See* 21 U.S.C. § 355(b)(1) (the [FDA] *shall publish* [the patent] information" submitted to it by the pioneer drug manufacturer in connection with a new drug application, if the application is approved)

> (emphasis added); *see also* 21 U.S.C. § 355(b)(2) (if the pioneer drug manufacturer was unable to file the patent information with the original application, because, for example, "the patent was issued after the [new drug] application was approved," it must file such patent information "not later than thirty days after the patent involved is issued," and "[upon submission of [this] patent information . . . , [FDA] *shall publish* it.") (emphasis added). In short, FDA plays only a ministerial role in the listing process. *See Abbott Laboratories v. Novopharm Ltd.*, 104 F.3d at 1307 n.1 ("[the FDA must accept as true the patent information supplied by the patentee, such as the patent expiration date").

App., *infra*, 162a. *See also Recent Developments Which May Impact Consumer Access to, and Demand for, Pharmaceuticals: Hearing before the Subcommittee on Health of the House Committee on Energy and Commerce,* 107th Cong. 4 (June 13, 2001) (prepared statement of Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration, Department of Health and Human Services) (hereinafter "*Recent Developments*") ("FDA does not undertake an independent review of the patents submitted by the NDA sponsor. FDA does not assess whether a submitted patent claims an approved drug and whether a claim of patent infringement could reasonably be made against an unauthorized use of the patented drug"). Rather, the FDA's view is that "[g]eneric and innovator firms may resolve any disputes concerning patents in private litigation." *Recent Developments*, *supra* at 4.

The FDA has maintained this position despite the express concerns of the original sponsors of the Hatch-Waxman Amendments, expressed in their August 17, 2001

letter to the FDA. *See* App., *infra*, 176a-177a (urging FDA to be "vigilant" in making certain that there is no gamesmanship by brand-name drug manufacturers to undermine entry into the market by generic drug manufacturers by allowing late issued patents to be listed in the Orange Book on the eve of generic competition).

As a result of the Federal Circuit's decision below and the established policies of the FDA, generic drug manufacturers like Mylan are unable to seek redress from the FDA or in judicial proceedings against the NDA holder/patent owner challenging the propriety of a patent-listing in the Orange Book. Consequently, there is no check on these practices by brand-name drug manufacturers, all to the harm of the public who will thereby be forced to deal with more rapidly escalating costs of prescription drugs.

## II. The Decision Below Contradicts Decisions of this Court Concerning Construction of the Hatch-Waxman Amendments and the Availability of Lack of a Cause of Action for Infringement Under 35 U.S.C. § 271(e)(2) as a Defense to Patent Infringement

The Hatch-Waxman Amendments were enacted in part "to make available more low-cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962." H. R. Rep. No. 98-857, pt. 1 at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647; *see also Eli Lilly & Co.*, 496 U.S. at 676. Congress struck a balance in 35 U.S.C. § 271(e) between the interests of generic drug manufacturers and manufacturers of patented drugs:

> On the one hand, the manufacture, use, or sale of a patented drug is not an act of infringement,

> to the extent it is necessary for the preparation and submission of an ANDA. On the other hand, once it is clear that a party seeking approval of an ANDA wants to market a patented drug prior to the expiration of the patent, the patent owner can seek to prevent approval of the ANDA by bringing a patent infringement suit.

Royce Lab., 69 F.3d at 1132.

In *Eli Lilly & Co.*, this Court addressed the issue of whether 35 U.S.C. § 271(e)(1) exempted certain activities in connection with the seeking of FDA approval of a medical device. *Eli Lilly & Co.*, 496 U.S. at 663. The Court construed 35 U.S.C. § 271(e)(2) to determine Congressional intent concerning the interplay of the relevant provisions of the Hatch-Waxman Amendments and concluded that their purpose was to create a "highly artificial act of infringement that consists of submitting an ANDA or a paper NDA *containing the fourth type of certification that is in error as to whether commercial manufacture, use, or sale of a new drug (none of which, of course, has actually occurred) violates the relevant patent*." *Eli Lilly & Co.*, 496 U.S. at 678 (emphasis added).

This artificial act of infringement under 35 U.S.C. § 271(e)(2) does not occur unless the NDA holder causes the FDA to list a patent in the Orange Book. The FDCA requires the ANDA applicant to file a certification for each patent listed in the Orange Book that claims the drug (or the use of the drug) for which it seeks approval. 21 U.S.C. Sec. 355(j)(2)(A) ("An abbreviated application for a new drug shall contain – (vii) a certification . . . with respect to each patent . . . for which information is required to be filed under subsection (b) or (c)

. . ."). Conversely, no certification is required in connection with patents that are not listed in the Orange Book. *Id.* ("The Secretary may not require that an [ANDA] contain information in addition to that required by clauses (i) through (viii)."). Thus, a proper Orange Book listing is the predicate for the artificial act of infringement that gives rise to a cause of action under § 271(e)(2). Improper listing (or non-listing or late listing) destroys that cause of action. *See also Ben Venue Labs., Inc. v. Novartis Pharm. Corp.*, 146 F. Supp. 2d 572, 582 (D.N.J. 2001) (court can adjudicate the § 271(e)(2) claim "so long as a Paragraph IV certification should have been included").

The issue in this case is whether an improper listing of a patent may be asserted as a defense in a declaratory judgment action in anticipation of an admittedly threatened action for infringement under 35 U.S.C. § 271(e)(2). If an improper listing does support such a defense, then ordering the delisting of the patent from the Orange Book was, as the District Court concluded, an appropriate remedy, thereby enabling the FDA to approve Mylan's ANDA immediately. The Federal Circuit, acknowledging that Mylan had raised "a matter of first impression for this court" (App., *infra*, 14a), answered this question in the negative. The district courts that have addressed this issue have reached conflicting conclusions. *Compare Ben Venue Lab. v. Novartis Pharm. Corp.*, 10 F. Supp. 2d 446 (D.N.J. 1998) (party may raise the issue of an improper Orange Book listing in an action for declaratory judgment), and *Abbott Lab. v. Zenith Lab.*, 934 F. Supp. 925, 936 (N.D. Ill. 1995) (holding that untimely filed patent-listing in Orange Book constituted defense for failure to state a claim under 35 U.S.C. § 271(e)(2)(A)), *dismissed without op.*, 78 F.3d 603 (Fed. Cir. 1996), with *Andrx Pharms., Inc. v. Biovail Corp.*, 175 F. Supp. 2d 1362, 1373 (S.D. Fla. 2001) (holding that no private right of action exists for declaratory judgment

that patent was improperly listed), *vacated and remanded on other grounds*, 276 F.3d 1368 (Fed. Cir. 2002).

The Court of Appeals ignored that only a proper listing would trigger the need to make a certification, thereby contravening this Court's statutory construction of 35 U.S.C. § 271(e)(2). The submission of an ANDA "containing the fourth type of certification" with respect to the "relevant patent," as explained in *Eli Lilly & Co.*, avoids the disablement of the patent holder from bringing a suit for infringement under 35 U.S.C. § 271(e)(1). *Eli Lilly & Co.*, 496 U.S. at 678. The Federal Circuit's ruling, if allowed to stand, would render the language qualifying "ANDA" in this Court's opinion superfluous. No Paragraph IV certification -- the artificial act of infringement -- is required for a patent that is not "relevant," and an improper listing would fall in that category.

Mylan's improper-listing defense against a threatened patent infringement action by Bristol under 35 U.S.C. § 271(e)(2) is essentially that Bristol cannot assert a cause of action under that statute. *Eli Lilly & Co.* supports that 35 U.S.C. § 271(e)(2) can only be invoked to entertain an infringement action under specific conditions; here, as Mylan established to the satisfaction of the District Court below, these conditions were not met because the patent-listing was improper (the '365 patent does not claim the approved drug or its use).

The relationship between the listing requirement of the FDCA and the requirements for a cause of action under § 271(e)(2) of the patent statute is apparent from the nearly identical language of the two provisions. The listing provision permits the listing of a patent "which claims the drug for which the application was submitted or which claims a method of using such drug." 21 U.S.C. § 355(c)(2). Under 35 U.S.C. §

271(e)(2), it is an act of infringement to submit an ANDA "for a drug claimed in a patent or the use of which is claimed in a patent." The close parallel of the language of these two statutory provisions provides further support for Mylan's position that a cause of action for infringement under § 271(e)(2) only exists for those patents that are properly listed in the Orange Book.

The Federal Circuit has repeatedly relied on the holding of *Eli Lilly & Co.* for the proposition that 35 U.S.C. § 271(e)(2) was a statutory grant of case or controversy jurisdiction to resolve a patent infringement claim brought by the owner of the patent in the pioneer drug. *See, e.g., Bayer AG*, 212 F.3d at 1249; *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997). In this respect, the Federal Circuit also ignored its own precedent in rejecting Mylan's argument.

The fact that the court below did not generally recognize a challenge to a plaintiff's right to assert a cause of action under the patent laws as falling within any of the categories of defenses to allegations of patent infringement demonstrates another conflict with the authority of this Court.[7]

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[7] The statutory defenses listed in 35 U.S.C. § 282 and referenced in the Federal Circuit's opinion are preceded by the following passage: "the following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded . . ." Section 282 does *not* specify that the enumerated defenses constitute an exclusive list of defenses in any action involving the validity or infringement of a patent. If Congress had intended such, the relevant language would read, "exclusive defenses." It is well-settled that "courts must presume that a legislature says in a statute what it means and means in a statute what it says there. . . . When the words of a statute are unambiguous, then, this first canon is also the last: judicial inquiry is complete." *Connecticut Nat'l Bank v. Germain*, 503 U.S. 249, 253-54 (1992) (internal quotation and citations omitted); *see Quantum Corp. v. Rodime, PLC*, 65 F.3d 1577, 1583-84 (Fed. Cir. 1995) (holding that

In interpreting 28 U.S.C. § 1338, this Court in *Christianson v. Colt Indus. Operating Corp.*, 486 U.S. 800 (1988), held that "the plaintiff must set up some right, title or interest under the patent laws, or at least make it appear that some right or privilege will be defeated by one construction, or sustained by the opposite construction of these laws." *Id.* at 807-808 (quoting *Pratt v. Harris Gas Lite and Coke Co.*, 168 U.S. 255, 259 (1897)). The decision below cited this exact language in *Christianson* but failed to take it into account in its analysis of whether Mylan was asserting a defense that arose under the patent laws. App., *infra*, 19a.

If, as Mylan contends, improper patent listing is appropriately raised as a defense to an action for infringement under 35 U.S.C. § 271(e)(2), then, under the "well-pleaded complaint rule," it also may be raised in an otherwise proper declaratory judgment action. *See Speedco*, 853 F.2d at 912.

## III. The Court Below Erred in Concluding that 21 U.S.C. §337(a) Bars a Generic Drug Manufacturer From Seeking Any Relief From an Improper Patent Listing in the Orange Book

The Federal Circuit's interpretation of the FDCA, specifically 21 U.S.C. § 337(a), disregards the plain language in that statute and is not supported by this Court's recent decision in *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001). This error on a matter of federal statutory construction further supports Mylan's request for review of the judgment below.

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the express words of § 282 allow for the existence of other invalidity defenses), *cert. denied*, 517 U.S. 1167 (1996).

The Federal Circuit held that because Mylan's action for declaratory judgment did not arise under the patent laws, 21 U.S.C. § 337(a) barred Mylan's declaratory judgment claim, because it rested on proving that Bristol improperly listed its patent in contravention of the requirements set forth in 21 U.S.C. § 355(c)(2). The court held: "In substance, Mylan's claim is analogous to those barred in the long line of cases precluding private rights of action under the FFDCA." App., *infra*, 18a-19a. The Federal Circuit concluded that neither the statute nor the legislative history revealed an intent to create a private right of action. App., *infra*, 18a. This interpretation does not fit the plain language of 21 U.S.C. § 337(a) and contravenes well-established rules of statutory construction.

Section 337(a) is the last of a series of sections in Subchapter III of the FDCA. It provides that "all *such* proceedings....shall be by and in the name of the United States." 21 U.S.C. § 337(a) (emphasis added). The word "such" limits the proceedings whose enforcement is reserved to the United States to those enumerated in the proceeding sections of Subchapter III, 21 U.S.C. §§ 331-336. These sections set forth a comprehensive list of proceedings for enforcing the safety and health provisions of the FDCA and make no reference to the enforcement of the patent laws or the patent-related provisions of the Hatch-Waxman Amendments.[8] "It is . . . a cardinal principle of statutory construction that we must give effect, if possible, to every clause and word of a statute." *Williams v. Taylor*, 529 U.S. 362, 404 (2000) (internal

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[8] Furthermore, 35 U.S.C. § 271(e)(2)(A) makes explicit reference to the statutory provisions of the FDCA concerning the ANDA approval process which strongly supports Mylan's assertion that an improper listing in the Orange Book arises under the patent laws and does not rely exclusively on enforcement of the FDCA, as the Federal Circuit held. App., *infra*, 18a.

quotations and citations omitted). Because 21 U.S.C. § 337(a) by its express terms is *not* an exclusive bar of every possible right of action that involves the Hatch-Waxman Amendments, the Federal Circuit's analysis is flawed. Moreover, a construction of § 337(a) that would reserve enforcement of the patent-listing requirements to the FDA would be inconsistent with the FDA's position that, under § 355(b)(1) and (c)(2), its role is merely ministerial with respect to those requirements. App., *infra*, 158a.

The Federal Circuit's statutory construction of § 337(a) is also not supported by this Court's recent decision in *Buckman Co. v. Plaintiffs' Legal Comm.*, *supra*. The Court of Appeals cited *Buckman Co.* among other authorities for the proposition that all private actions to enforce any provision of the FDCA are barred by 21 U.S.C. § 337(a). App., *infra*, 14a. This Court's opinion in *Buckman Co.* did not so hold. Rather, this Court held that: "[the FDCA leaves no doubt that it is the Federal Government rather than private litigants who are authorized to file suit for non-compliance *with the medical device provisions....*" *Buckman Co.*, 531 U.S. at 349 n.4 (emphasis added). The opinion refers to specific sections of Subchapter III of the FDCA (21 U.S.C. § 332; 21 U.S.C. § 333(f)(1)(A); 21 U.S.C. § 334(a)(2)(D)) covering FDA's statutory enforcement options concerning medical devices. *Buckman Co.*, 531 U.S. at 349. Because Subchapter III contains no provisions relating to the patent provisions of the FDCA, this Court's decision in *Buckman Co.* does not support a conclusion that 21 U.S.C. § 337(a) bars an action seeking a declaration that no cause of action under § 271(e)(2) exists based on a patent listing in the

Orange Book.[9] This important issue of federal statutory construction provides a further basis for the grant of certiorari.

## CONCLUSION

For the foregoing reasons, Mylan respectfully requests that its petition for a writ of certiorari be granted.

Respectfully submitted,

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[9] Subchapter III has been amended since enactment of the Hatch-Waxman Amendments. Therefore, Congress had an opportunity to include the patent-listing provisions of the FDCA in those provisions whose enforcement was reserved to the federal government had it chosen to do so. It did not. It would be illogical to reserve enforcement of the patent provisions of the FDCA to the FDA, given the agency's lack of expertise in patent matters.

# APPENDIX

# United States Court of Appeals for the Federal Circuit

01-1257

MYLAN PHARMACEUTICALS, INC.,

Plaintiff-Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services,
BERNARD A. SCHWETZ, D.V.M., Ph.D, Acting Principal Deputy Commisssioner,
U.S. Food and Drug Administration, and U.S. FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,
and

BRISTOL-MYERS SQUIBB COMPANY,

Defendant-Appellant.

E. Anthony Figg, Rothwell, Figg, Ernst & Manbeck, P.C. of Washington, DC, argued for plaintiff-appellee. With him on the brief were Steven M. Lieberman and Elizabeth A. Leff.

Howard S. Scher, Attorney, Appellate Staff, Civil Division, Department of Justice, of Washington, DC, argued for defendants-appellees. With him on the brief were Stuart E. Schiffer, Acting Assistant Attorney General; and

Douglas N. Letter, Attorney. Of counsel on the brief were Michael M. Landa, Acting Chief Counsel; and Kevin M. Fain, Associate Chief Counsel, Office of the Chief Counsel, U.S. Food and Drug Administration, of Rockville, Maryland.

Evan R. Chesler, Cravath, Swaine & Moore, of New York, New York, argued for defendant-appellant. With him on the brief was Richard J. Stark. Of counsel were David R. Marriott, Swaine & Moore; and Mathew D. Peterson, FoxKiser, of Washington, DC.

Richard A. Samp, Washington, Legal Foundation, of Washington, DC, for amicus curiae Washington Legal Foundation. With him on the brief was Daniel J. Popeo.

Appealed from: United States District Court for the District of Columbia

Judge Ricardo M. Urbina

# United States Court of Appeals for the Federal Circuit

01-1257

MYLAN PHARMACEUTICALS, INC.,

Plaintiffs-Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services,
BERNARD A. SCHWETZ, D.V.M., Ph.D., Acting Principal Deputy
Commissioner, U.S. Food and Drug Administration,
and U.S. FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

v.

BRISTOL-MYERS SQUIBB COMPANY,

Defendant-Appellant.

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DECIDED: October 12, 2001

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Before MAYER, Chief Judge, NEWMAN and MICHEL, Circuit Judges.

MAYER, Chief Judge.

Bristol-Myers Squibb Co. ("Bristol") appeals the order of the United States District Court for the District of Columbia granting the motion for a preliminary injunction brought by Mylan Pharmaceuticals, Inc. ("Mylan"). See Mylan Pharms., Inc. v. Thompson, No. 00-2876 (D.D.C. Mar. 14, 2001). The injunction directed Bristol to take measures to delist United States Patent No. 6,150,365 from the U.S. Food and Drug Administration's "Orange Book," and directed the FDA to grant final approval of Mylan's abbreviated new drug application for a generic version of buspirone. Id. Because we find that such a declaratory relief action against Bristol was not available to Mylan under the patent laws and was not created by the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act ("FFDCA") and to Title 35 of the United States Code, we reverse.

## Regulatory Background

This case turns on the statutory framework governing new and generic drug approvals and its mechanisms for patent enforcement. Under the FFDCA, a pharmaceutical company seeking to manufacture a new drug is required to file a New Drug Application ("NDA") for consideration by the FDA. 21 U.S.C. § 355(a) (1994). Preparing an NDA is frequently a time-intensive and costly process, because among other things, it must contain detailed clinical studies of the drug's safety and efficacy. See id. § 355(b)(1) (Supp. V 1999). The NDA must also include a list of patents which claim the drug:

> The applicant shall file with the

> application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. . . . Upon approval of the application, the Secretary shall publish information submitted under [this section].

Id.

If the FDA approves the NDA, it publishes a listing of the drug and patents on the drug's approved aspects in Approved Drug Products with Therapeutic Equivalence Evaluations, otherwise known as the "Orange Book." Id. § 355(j)(7)(A)(iii) (1994); id. § 355(b)(1); see also 21 C.F.R. § 314.53(c)(2) (2001). Because an applicant may not receive original approval for all aspects of the drug as described in the original NDA submission, once the NDA is approved, the applicant must amend the patent submission to list only the patents that meet the listing criteria for the approved drug product. 21 C.F.R. § 314.53(c)(2)(ii) (2001).

Under the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984), codified at 21 U.S.C. §§ 355, 360cc, and 35 U.S.C. §§ 156, 271, 282 (the "Hatch-Waxman Amendments" to the FFDCA and to Title 35 of the U.S. Code relating to patents), a

pharmaceutical manufacturer seeking approval to market a generic version of a previously approved drug may submit an abbreviated new drug application ("ANDA") to the FDA. 21 U.S.C. § 355(j) (1994). An ANDA offers an expedited approval process for generic drug manufacturers. Instead of filing a full NDA with new safety and efficacy studies, in an ANDA a generic manufacturer may rely in part on the pioneer manufacturer's work by submitting data demonstrating the generic product's bioequivalence with the previously approved drug. See id. § 355 (j)(2)(A) (Supp. V 1999). These provisions of the Hatch-Waxman Amendments "emerged from Congress' efforts to balance two conflicting policy objectives: to induce name brand pharmaceutical firms to make the investments necessary to research and develop new drug products, while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market." Abbott Labs. v. Young, 920 F.2d 984, 991 (D.C. Cir. 1990) (Edwards, J., dissenting on other grounds). Thus, Title I of the Act was intended to "make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962." H.R. Rep. No. 98-857, pt. 1 at 14 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2647. Title II, on the other side of the scale, was intended to benefit pioneer drug manufacturers by "restor[ing] . . . some of the time lost on patent life while the product is awaiting pre-market approval." H.R. Rep. No. 98-857, pt. 1 at 15, 1984 U.S.C.C.A.N. at 2648.

The Hatch-Waxman provisions concerning patent infringement are part of this balance. Under 35 U.S.C. § 271(e)(1), it is not infringement to conduct otherwise infringing acts necessary to prepare an ANDA. 35 U.S.C. § 271(e)(1) (Supp. V 1999) ("It shall not be an act of infringement to make, use, offer to sell, or sell . . . a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal

law which regulates the manufacture, use, or sale of drugs."). Under section 271(e)(2), however, a generic drug manufacturer infringes by filing an ANDA to obtain FDA approval for the purpose of marketing a generic drug product claimed in a patent before the patent expires. 35 U.S.C. § 271(e)(2) (1994) ("It shall be an act of infringement to submit . . . [an ANDA] . . . if the purpose of such submission is to obtain [FDA] approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent before the expiration of such patent.") (emphasis added). Despite this provision, not all ANDA applicants can be sued immediately for infringement; moreover, they cannot sue immediately for declaratory judgment with respect to the patent, as further discussed below.

As part of the ANDA process, an applicant seeking to market a generic version of a listed drug must make a certification as to each patent listed in the Orange Book which "claims the listed drug . . . or which claims a use for such listed drug for which the applicant is seeking approval." 21 U.S.C. § 355(j)(2)(A)(vii) (1994). Further, according to regulations enacted by the FDA, an applicant whose ANDA is pending when a pioneer drug manufacturer lists additional patents in the Orange Book must make certifications as to the new patents, unless the additional patents are submitted more than thirty days after they were issued. 21 C.F.R. § 314.94(a)(12)(vi) (2001).

In either case, the applicant must certify either that: (I) no such patent information has been submitted to the FDA; (II) the patent has expired; (III) the patent is set to expire on a certain date; or (IV) such patent is invalid or will not be infringed by the manufacture, use, or sale of the new generic drug for which the ANDA is submitted. 21 U.S.C. § 355(j)(2)(A)(vii)(I-IV) (1994). These are commonly referred to as Paragraph I, II, III, and IV certifications. Further, if one of the listed patents is a method-of-use patent which does not

claim a use for which the applicant is seeking approval, the applicant must make a statement to that effect (a "Section viii Statement"). Id. § 355(j)(2)(A)(viii).

An ANDA containing a Paragraph I or II certification may be approved without additional delay. See 21 U.S.C. § 355(j)(5)(B)(i) (Supp. V 1999). An ANDA containing a Paragraph III certification indicates that the applicant does not intend to market the drug until after the expiration of the patent, and the approval of the ANDA cannot be made final until the patent expires. Id. § 355(j)(5)(B)(ii).

When an ANDA contains a Paragraph IV certification, the ANDA applicant must give notice to the patentee and must provide detailed bases for its belief that the patent is invalid, unenforceable, or not infringed. Id. § 355(j)(2)(B)(i); 21 C.F.R. § 314.95(c)(6) (2001). The patentee is then given forty-five days to sue the ANDA applicant for infringement. 21 U.S.C. § 355(j)(5)(B)(iii) (Supp. V 1999). If the patentee does not file suit, the application may be approved. If the patentee files suit within that period, the FDA may not approve the ANDA until the expiration of the patent, judicial resolution of the infringement suit, a judicial determination that the patent is invalid or unenforceable, or thirty months from the patentee's receipt of notice, whichever is earliest. Id.; 21 C.F.R. § 314.107(b)(1)(iv) (2001). The court in which the suit is pending may order a shorter or longer stay on the approval time if "either party to the action fail[s] to reasonably cooperate in expediting the action." 21 U.S.C. § 355(j)(5)(B)(iii) (Supp. V 1999). Moreover, the availability of declaratory judgment actions is limited: "Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of Title 28, for a declaratory judgment with respect to the patent." Id. These provisions give the pioneer manufacturer the first opportunity to file suit against the ANDA applicant for infringement, and

may substantially delay the ANDA approval during the pendency of the litigation.

The Hatch-Waxman Amendments, however, do not include any explicit provisions either enabling or prohibiting an action to challenge a patentee's listing of a patent in the Orange Book. By regulation, the FDA has provided a limited process for disputing the accuracy or relevance of patent information submitted to the FDA and listed in the Orange Book. 21 C.F.R. § 314.53(f) (2001). One who questions the accuracy of the patent information may write to the FDA, and the FDA will request that the applicant confirm the information. Id. According to the FDA's regulations, however, "[u]nless the application holder withdraws or amends its patent information in response to FDA's request, the agency will not change the patent information in the list" and an ANDA applicant must still make certifications for each patent despite its disagreement. Id.

Factual Background

Bristol owns U.S Patent No. 4,182,763 ("'763 patent") directed to the treatment of anxiety through the administration of buspirone hydrochloride. The '763 patent is listed in the Orange Book as covering Bristol's FDA-approved drug "BuSpar." Bristol's patent was set to expire at the end of the day on November 21, 2000. In anticipation of its expiration, Mylan, a generic manufacturer, had filed and received tentative approval of an ANDA for its buspirone product under a Paragraph III certification. Mylan manufactured and was ready to ship its product at 12:00 a.m. on November 22, 2000, the moment the '763 patent was to have expired.

Approximately eleven hours before the '763 patent's expiration, Bristol hand-delivered to the FDA copies of U.S. Patent No. 6,150,365 (the "'365 patent") which issued earlier

that day. The '365 patent contains only one claim, directed towards:

> A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of . . . [BMY 28674 (the active metabolite of buspirone)] or a pharmaceutically acceptable acid addition salt or hydrate thereof.

'365 patent, col. 16, ll. 27-32. Bristol sought to have the '365 patent listed in the Orange Book as covering buspirone.

Upon receiving the '365 patent from Bristol, the FDA suspended approval of Mylan's ANDA and the ANDAs filed by other prospective generic manufacturers of buspirone. Mylan and other ANDA applicants wrote to the FDA to challenge the listing of the '365 patent on the grounds that it only covered a metabolite of buspirone and therefore should not be listed because it did not claim the drug, citing our ruling in Hoechst-Roussel Pharmaceuticals, Inc. v. Lehman, 109 F.3d 756, 42 USPQ2d 1220 (Fed. Cir. 1997). Mylan also filed a Section viii Statement that the '365 patent did not claim a use for which it was seeking approval.

The FDA responded on November 30, 2000, by asking Bristol to provide a clarification as to whether the '365 patent claimed only a metabolite of buspirone. The FDA also requested additional information from the ANDA applicants concerning the effect of our Hoechst ruling on the '365 patent claim. Bristol responded that the '365 patent did not simply claim a method of using the metabolite, but also a method of

using buspirone itself. The FDA informed Bristol that its response was adequate and that the '365 patent would be deemed listed in the Orange Book.

Instead of filing a Paragraph IV certification with respect to the ANDA at issue here, Mylan commenced the present action against Bristol and the FDA on the same day, November 30, 2000. It sought a declaratory judgment that Bristol improperly listed the '365 patent, and a preliminary injunction requiring Bristol to take steps to delist the '365 patent and directing the FDA to approve Mylan's ANDA. Mylan also filed an action in the United States District Court for the District of West Virginia for a declaration of noninfringement and invalidity, and Bristol sued Mylan for infringement in the Southern District of New York.

In the present action, the United States District Court for the District of Columbia held that Mylan was entitled to declaratory relief that the '365 patent was improperly listed in the Orange Book under the patent laws and the Declaratory Judgment Act, as a defense to the infringement suit Bristol could have brought against Mylan under 35 U.S.C. § 271(e)(2). Mylan, slip op. at 18-27. It held that it possessed subject matter jurisdiction over the case under the patent laws, and that Mylan was not attempting to enforce the FFDCA against Bristol. Id. at 17-18. The court proceeded to review the '365 patent's claim, specification, and prosecution history, and found that the '365 patent did not claim the drug for which the applicant submitted the application or claim a method of using such drug upon which a claim of patent infringement could reasonably be asserted. Id. at 29-44 (applying 21 U.S.C. § 355(b)(1)(F) (1994)). It therefore held that Mylan was likely to succeed on the merits of its claim. See Mylan, slip op. at 45. Although the court said that Mylan made no showing of irreparable harm, it granted the injunction. Id. at 48, 50-51.

Bristol appeals the district court's order. Although the FDA opposed Mylan's motion in the district court, stating that its role in listing patents was solely ministerial and that Mylan's remedy was to seek modification of the presumptive thirty-month stay in the infringement litigation, id. at 16, the FDA does not appeal the portion of the order directing it to approve Mylan's ANDA. Instead, the FDA argued to this court that this portion of the order was harmless error, and that Mylan has a cognizable cause of action against Bristol for declaratory judgment under the patent laws that was not prohibited by the FFDCA. We therefore do not address any cause of action that Mylan has or may assert against the FDA.

## Discussion

The grant or denial of a preliminary injunction under 35 U.S.C. § 283 is within the sound discretion of the district court. Purdue Pharma L.P. v. Boehringer Ingelheim Gmbh, 237 F.3d 1359, 1363, 57 USPQ2d 1647, 1649 (Fed. Cir. 2001) (citations omitted).[1] An abuse of discretion may be established

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[1] We apply the law of the regional circuit to which the district court appeal normally lies unless "the issue pertains to or is unique to patent law," in which case we will apply our own law to both substantive and procedural issues "intimately involved in the substance of enforcement of the patent right." Amana Refrigeration, Inc. v. Quadlux, Inc., 172 F.3d 852, 856-57, 50 USPQ2d 1304, 1307 (Fed. Cir. 1999) (citations omitted) (affirming district court's analysis of personal jurisdiction on state law trade libel and defamation claims under Eighth Circuit law and analyzing mootness of declaratory judgment of patent invalidity and noninfringement under Federal Circuit law). Here, the questions of choice of law and the existence of declaratory relief are intertwined. Because the issues of law underlying the preliminary injunction are "intimately involved in the substance of enforcement of the patent right," namely, Bristol's ability to list and enforce its patent rights under the mechanisms provided under the Hatch-Waxman Amendments, we will apply Federal Circuit law. We note that the parties have cited cases from both the D.C. Circuit and the Federal Circuit, and have not

by showing that the court made a clear error of judgment in weighing relevant factors or exercised its discretion based upon an error of law or clearly erroneous factual findings. Id.; Amazon.com, Inc. v. barnesandnoble.com, Inc., 239 F.3d 1343, 1350, 57 USPQ2d 1747, 1751 (Fed. Cir. 2001) (citing Novo Nordisk of N. Am., Inc. v. Genentech, Inc., 77 F.3d 1364, 1367, 37 USPQ2d 1773, 1775 (Fed. Cir. 1996)). To the extent that a district court's decision to grant a preliminary injunction hinges on questions of law, our review is de novo. See Globetrotter Software, Inc. v. Elan Computer Group, Inc., 236 F.3d 1363, 1367, 57 USPQ2d 1542, 1545 (Fed. Cir. 2001).

As the moving party, Mylan was required to establish its right to a preliminary injunction in light of four factors: "(1) a reasonable likelihood of success on the merits; (2) irreparable harm if the injunction were not granted; (3) the balance of the hardships and (4) the impact of the injunction on the public interest." Purdue, 237 F.3d at 1363, 57 USPQ2d at 1649 (citing Polymer Techs. v. Bridwell, 103 F.3d 970, 973, 41 USPQ2d 1185, 1188 (Fed. Cir. 1996)). If we find that Mylan was not likely to succeed on the merits, we may reverse the injunction. Reebok Int'l Ltd. v. J. Baker, Inc., 32 F.3d 1552, 1556, 32 USPQ2d 1781, 1785 (Fed. Cir. 1994).

With respect to the first factor, Bristol argues that the district court erred because Mylan did not assert a cognizable cause of action. According to Bristol, Mylan's claim seeks to delist a patent from the Orange Book, which is an impermissible attempt by a private party to enforce the FFDCA. See 21 U.S.C. § 337(a) (1994) ("Except as provided in subsection (b) of this section [regarding suits by states in their own names], all such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the

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pointed to any material difference between the circuits with respect to the substantive requirements for a preliminary injunction and its standards of review.

name of the United States."); see also Buckman Co. v. Plaintiffs' Legal Comm., 121 S.Ct. 1012, 1017, 1018 n.4, 1019 (2001); In re: Orthopedic Bone Screw Prods. Liab. Litig., 193 F.3d 781, 788 (3d Cir. 1999) ("It is well settled . . . that the FDCA creates no private right of action."). Therefore, Bristol argues that granting declaratory relief is improper because, under the well-pleaded complaint rule, Bristol would have no cause of action against Mylan to "list" the '365 patent.

Mylan and the FDA concede that there is no cause of action to delist a patent from the Orange Book. They also concede that such an action would be a private right of action barred by the FFDCA. They submit, however, that Mylan's cause of action, and the basis for our jurisdiction and declaratory relief, arises under the patent laws as a defense to patent infringement.

This is a matter of first impression for this court. The Declaratory Judgment Act, 28 U.S.C. § 2201, is remedial only. It "enlarged the range of remedies available in the federal courts but did not extend their jurisdiction." Skelly Oil v. Phillips Petroleum Co., 339 U.S. 667, 671 (1950). A party's legal interest under the Act must relate to an actual "claim arising under federal law which another asserts against him . . . ." Lowe v. Ingalls Shipbuilding, A Div. of Litton, 723 F.2d 1173, 1179 (5th Cir. 1984). Because it is "the underlying cause of action of the defendant against the plaintiff that is actually litigated in a declaratory judgment action, a party bringing a declaratory judgment action must have been a proper party had the defendant brought suit on the underlying cause of action." Collin County, Tex. v. Homeowners Ass'n for Values Essential to Neighborhoods (HAVEN), 915 F.2d 167, 171 (5th Cir. 1990). Therefore, we are required to identify the federal law under which Mylan is proceeding.

Applying the "well-pleaded complaint rule" for

analyzing a purported declaratory judgment, we do not look to the plaintiff's complaint to determine which federal law is the basis of the declaratory plaintiff's cause of action, "but to the action that the declaratory defendant would have brought" to enforce its rights. Speedco, Inc. v. Estes, 853 F.2d 909, 912, 7 USPQ2d 1637, 1640 (Fed. Cir. 1988); see Fina Oil and Chem. Co. v. Ewen, 123 F.3d 1466, 1470, 43 USPQ2d 1935, 1938 (Fed. Cir. 1997) ("We apply [the well-pleaded complaint rule] not to the declaratory judgment complaint but to the hypothetical action the declaratory defendant would have brought.") Although in Speedco and Fina we used this rule to determine whether the district court had subject matter jurisdiction, the principles also are helpful for determining which federal law is the basis for the declaratory plaintiff's cause of action.

Mylan argues that the action Bristol, the declaratory judgment defendant, would have brought is an action for patent infringement under 35 U.S.C. § 271(e)(2). This section provides that an applicant infringes a patent if it submits an ANDA "for a drug claimed in a patent or the use of which is claimed in a patent . . . before the expiration of such patent." 35 U.S.C. § 271(e)(2) (1994). Mylan argues that had it filed an ANDA with a Paragraph IV certification, it would have been charged with infringing the '365 patent. One of the defenses, which Mylan argues would be available to it in Bristol's hypothetical patent infringement suit, is that Mylan should not have been required to file a Paragraph IV certification in the first instance because the '365 patent did not claim BuSpar or an approved method of using BuSpar, and accordingly, Bristol improperly submitted the '365 patent for listing in the Orange Book.

This assertion, however, is not a recognized defense to patent infringement. Defenses to allegations of patent infringement fall into two broad groups: statutory and

equitable. The statutory defenses are set forth in 35 U.S.C. § 282 and include non-infringement, absence of liability for infringement, unenforceability, and invalidity (for failure to meet the conditions of patentability or to comply with any requirement of sections 112 or 251). 35 U.S.C. § 282 (Supp. V 1999). The equitable defenses include unclean hands, unenforceability of the patent for fraud and inequitable conduct, misuse, and delay in filing suit resulting in laches or estoppel. See E.B. Lipscomb III, Lipscomb's Walker on Patents, § 261:1 (3d. ed. 1988); c.f. J.P. Stevens & Co. v. Lex Tex, Ltd., 747 F.2d 1553, 1561, 223 USPQ 1089, 1093 (Fed. Cir. 1984) (stating that 35 U.S.C. section 282 paragraph 1 incorporates equitable defenses).

Mylan does not tie its argument to any of these defenses. The issue that Mylan seeks to litigate under this declaratory judgment action is not infringement of the '365 patent, i.e., that Mylan did not infringe under 35 U.S.C. § 271(e)(2)(A) because its ANDA was not "for a drug claimed in the patent or the use of which is claimed in a patent." Instead, it seeks to litigate whether Bristol is barred from asserting the '365 patent against any ANDA applicant because Bristol did not properly comply with the listing requirements set forth in the FFDCA. Although this issue may be akin to an estoppel defense or an unenforceability defense for a patentee's inequitable conduct in prosecuting a patent in the Patent and Trademark Office, Mylan has not asserted any such link.

Because the Hatch-Waxman Amendments create the statutory act of infringement here, however, we should also examine them to determine whether they add an additional defense.[2] A review of the amendments shows no explicit

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[2] The Hatch-Waxman Amendments were made both to the FFDCA and to Title 35 of the United States Code relating to patents. As such, a number of the Hatch-Waxman Amendments constitute part of the patent laws, and are essential to defining whether a defense to

provisions allowing an accused infringer to defend against infringement by challenging the propriety of the Orange Book listing of the patent. Section 271(e)(4) authorizes specific remedies available to the patentee for the act of infringement of submitting an ANDA, but does not contemplate any remedies to the accused applicant (except, perhaps, for attorney fees under 35 U.S.C. § 285). 35 U.S.C. § 271(e)(4) (1994).

The only explicit statement in the amendments concerning an applicant's rights to seek judicial relief against the patentee is in 21 U.S.C. § 355(j)(5)(B)(iii)(III). This section provides that no one, including the ANDA holder, may commence "an action . . . for declaratory judgment with respect to the [listed] patent" before the expiration of forty-five days from the date the patent owner receives notice of the ANDA holder's Paragraph IV certification. 21 U.S.C. § 355(j)(5)(B)(iii) (Supp. V 1999). Mylan and the FDA argue that this rule does not apply to Mylan's declaratory judgment action. They argue that section 355(j)(5)(B)(iii)'s reference to an "action" must be read in a manner consistent with the prior references to "action," "an action," or "such an action" in the remainder of the section and the amendments. Therefore, the type of "action" referred to here is one for infringement under 35 U.S.C. § 271(e)(2)(A), responding to a Paragraph IV certification that the patent is invalid, unenforceable, or will not be infringed. See 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (1994); 21 C.F.R. § 314.107(b)(3) (2001). Because an allegation that a patent is improperly listed does not raise any of these issues, Mylan asserts that its claim here is not an "action" covered by this forty-five day exclusion rule.

Mylan's arguments further bolster our conclusion that its claim is not a recognized defense to patent infringement. There is no indication in 21 U.S.C. § 355(j)(5)(B)(iii)(III) that

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infringement is available under 35 U.S.C. § 271(e)(2)(A).

Congress intended to provide an additional defense. Instead it indicates that Congress only envisioned that recognized defenses could be raised in declaratory judgments in patent infringement actions. See 21 C.F.R. § 314.107(b)(3) (2001) (expanding Paragraph IV certification to include "unenforceability" defense in addition to the invalidity and noninfringement defenses stated in 21 U.S.C. § 355(j)(2)(A)(vii)(IV), because unenforceability is a recognized reason why a generic drug product would not violate a patent holder's rights); see also Merck v. Danbury Pharmacal, Inc., 873 F.2d 1418, 10 USPQ2d 1682 (Fed. Cir. 1989) (applying unenforceability as a defense in the section 355 context); 59 Fed. Reg. at 50339. Finally, the parties have shown nothing in the scant legislative history of the amendments pointing to an intent to provide such a defense, or to create a private action for delisting a patent from the Orange Book for a patentee's failure to comply with section 355.

Therefore, we are forced to conclude that Mylan's action here against Bristol is in essence an attempt to assert a private right of action for "delisting" under the FFDCA. We see nothing in the Hatch-Waxman Amendments to alter the statement in section 337(a) of the FFDCA that "all such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States." 21 U.S.C § 337(a) (1994). "In a case in which neither the statute nor the legislative history reveals a congressional intent to create a private right of action for the benefit of the plaintiff," the inquiry is at an end. Northwest Airlines, Inc. v. Transp. Workers, 451 U.S. 77, 94 n.31 (1981). Mylan is not merely using the standards enunciated by the FFDCA to support an independent cause of action (as in the district court cases Mylan cites). Instead, its entire cause of action rests on proving that Bristol improperly listed the '365 patent because it does not comply with the requirements of 21 U.S.C. § 355(b)(1). In substance, Mylan's claim is analogous to those

barred in the long line of cases precluding private rights of action under the FFDCA. See In re Orthopedic Bone Screw Prods. Liab. Litig., 193 F.3d at 790 ("A claim of civil conspiracy cannot rest solely upon the violation of a federal statute for which there is no corresponding private right of action."); see also Mylan Labs., Inc. v. Matkari, 7 F.3d 1130, 1139 (4th Cir. 1993) ("We agree with the defendants that permitting Mylan to proceed on the theory that the defendants violated § 43(a) merely by placing their drugs on the market would, in effect, permit Mylan to use the Lanham Act as a vehicle by which to enforce the Food, Drug, and Cosmetic Act ("FDCA") and the regulations promulgated thereunder. An attempt, by ingenious pleading, to escape one principle of law by making it appear that another not truly appropriate rule is applicable appears to have been attempted.").[3]

Our cases do not suggest a different result. In Abbott Laboratories v. Novopharm Ltd., 104 F.3d 1305, 1309, 41 USPQ2d 1535, 1538 (Fed. Cir. 1997), we held that, as part of its inherent power to give effect to a judgment, a court may order the delisting of a patent in the context of a properly filed patent infringement suit. Abbott and its rationale, however, do not provide us the authority to hear an independent cause of action seeking delisting outside a properly filed patent case. In

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[3] Our conclusion that a declaratory relief action to "delist" is unavailable under the patent laws does not preclude jurisdiction. The determination of whether federal patent law creates such a remedy invokes our jurisdiction per Christianson v. Colt Industries Operating Corp., 486 U.S. 800, 7 USPQ2d 1109 (1988). Jurisdiction under 28 U.S.C. § 1338 extends to those cases in which a well-pleaded complaint establishes "that the plaintiff's right to relief necessarily depends on resolution of a substantial question of federal patent law." Id. at 809, 7 USPQ2d at 1113. Resolution favoring the plaintiff is not required for jurisdiction, because a case arises under the federal patent laws if the "'plaintiff set[s] up some right, title or interest under the patent laws, or at least make[s] it appear that some right or privilege will be defeated by one construction, or sustained by the opposite construction of these laws.'" Id. at 807-08, 7 USPQ2d at 1113 (quoting Pratt v. Paris Gas Light & Coke Co., 168 U.S. 255, 259 (1897)).

DuPont Merck Pharmaceutical Co. v. Bristol-Myers Squibb Co., 62 F.3d 1397, 35 USPQ2d 1718 (Fed. Cir. 1995), we held that an actual controversy was presented under the Declaratory Judgment Act where the declaratory judgment plaintiffs sought a declaration as to whether and how a specific statutory safe harbor relating to equitable remuneration in lieu of damages for infringement suits would apply to them. In Dupont, unlike here, there was no question that the statutory safe harbor and remuneration provisions were remedies responsive to would-be infringement claims.

Notably, Congress has considered legislation to amend the FFDCA to loosen the restrictions on generic ANDA applicants under 21 U.S.C. § 355(j)(5). See Greater Access to Affordable Pharmaceuticals Act of 2001, S. Res. 812, 107th Cong. (2001). The bill proposes, among other things, amending the forty-five day rule to allow a declaratory judgment with respect to the patent such that "if information on a patent for a listed drug has been published under subsection (c)(2) for at least 1 year after the date on which an abbreviated application for approval of a new drug was filed under this subsection in relation to the listed drug, the person that filed the abbreviated application or the holder of the approved application for the listed drug may immediately bring a civil action to determine the legal status of the patent for the listed drug." This provision appears to recognize Mylan's cause of action, subject to a one-year time delay from the publication of the patent information. It reinforces our conclusion that neither the general patent laws nor the Hatch-Waxman Amendments now permit Mylan's asserted action against Bristol in this case.[4]

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[4] Because our review of the above issues disposes of the case, we need not address the remainder of the arguments submitted by the parties.

## Conclusion

Accordingly, the judgment of the United States District Court for the District of Columbia is reversed.

REVERSED

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

01-1257

MYLAN PHARMACEUTICALS, INC.,

Plaintiff-Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services, BERNARD A. SCHWETZ, D.V.M., Ph.D., Acting Principal Deputy Commissioner, U.S. Food and Drug Administration, and U.S. FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

v.

BRISTOL-MYERS SQUIBB COMPANY,

Defendant-Appellant.

# Judgment

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|---|---|
| ON APPEAL from the | UNITED STATES DISTRICT COURT DISTRICT OF COLUMBIA |
| In CASE NO(S). | 00-CV-2876 |

This CAUSE having been heard and considered, it is

ORDERED and ADJUDGED:

REVERSED

ENTERED BY ORDER OF THE COURT

DATED Oct. 12, 2001 Jan Horbaly, Clerk

ISSUED AS A MANDATE: JANUARY 16, 2002

**UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF COLUMBIA**

| | | |
|---|---|---|
| MYLAN PHARMACEUTICALS, INC., | : | |
| Plaintiff, | : | |
| | : | Civil Action |
| v. | : | No.: 00-2876 (RMU) |
| TOMMY G. THOMPSON, Secretary, United States Department of Health and Human Services, United States Food and Drug Administration, | : | Document Nos.: 3, 4 |
| and | : | |
| BRISTOL-MYERS SQUIBB CO., | : | |
| Defendants. | : | |

**MEMORANDUM OPINION**
**GRANTING THE PLAINTIFF'S REQUEST FOR A PRELIMINARY INJUNCTION**

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## I. INTRODUCTION

Mylan Pharmaceuticals, Inc., a generic drug manufacturer, moves for a preliminary injunction ordering defendant Bristol-Myers Squibb Co. ("Bristol" or "BMS") to de-list U.S. Patent No. 5,150,365 ("the `365 patent") from the United States Food and Drug Administration ("FDA")'s "Orange Book" and directing the FDA to approve immediately Mylan's Abbreviated New Drug Application ("ANDA") No. 75-252. Bristol's `365 patent covers a method of using BuSpar®, Bristol's brand-name buspirone hydrochloride ("buspirone") product. Mylan seeks this preliminary injunction so that it may proceed with plans to sell its generic buspirone product. For the reasons that follow, the court will grant Mylan's request for a preliminary injunction.

## II. STATUTORY FRAMEWORK: THE HATCH-WAXMAN ACT

### A. Pioneer Makers and New Drug Applications (NDAs)

An understanding of the statutory and regulatory framework governing the approval of generic drugs is critical to assessing the merits of the parties' claims. The Federal Food, Drug, and Cosmetic Act ("FFDCA"), as amended by the Drug Price Competition and Patent Term Restoration Act of 1984, authorizes the FDA to regulate the production, distribution, and sale of drugs in the United States. See 21 U.S.C. §§ 321-397. An applicant seeking to market a new brand-name drug ("a pioneer maker") must prepare a

rigorous New Drug Application ("NDA") for FDA consideration. See 21 U.S.C. § 355. The NDA contains reports of the drug's safety and effectiveness, a list of the articles used as components in the drug, a statement of the composition of the drug, a description of the methods, facilities and controls used in the manufacture, processing and packaging of the drug, samples of the drug or components, if necessary, and samples of the proposed labeling. *See* 21 U.S.C. § 355(b)(1). In addition, the NDA must contain information on any patents that claim the drug or a method of using the drug and for which a claim of patent infringement could reasonably be asserted against an unauthorized party. *See* 21 U.S.C. §§ 355(b)(1), (c)(2).[1]

Upon approval of the NDA, the FDA publishes any claimed patents for the approved drug in "Approved Drug Products with Therapeutic Equivalence Evaluations," also known as the "Orange Book." *See* 21 U.S.C. § 355(j)(7)(A)(iii). Pioneer makers have considerable incentive to cause the FDA to list patents in the Orange Book. *See* Mylan's Memorandum of Law in Support of its Motion for Preliminary Injunction ("Mot. for Prelim. Inj.") at 12 (citing *Bristol- Myers Squibb Co. v. Ben Venue Labs.*, 90 F. Supp.2d 522, 524 (D.N.J. 2000)). When the FDA lists a patent for an approved drug, generic makers often have to wait an additional thirty months to obtain FDA approval of their competing generic drugs. *See* Mot. for Prelim. Inj. at 12.

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[1] FDA regulations define the types of patents that may be submitted in conjunction with an NDA: drug substance (active ingredient) patents; drug product (formulation and composition) patents; and method-of-use patents. *See* 21 C.F.R. § 314.53(b). For patents covering the formulation, composition, or method of using a drug, the NDA applicant also must submit a signed declaration stating that the patent covers the formulation, composition, or use of the product described in the pending or approved application. *See* 21 C.F.R. § 314.53(c)(2).

### B. Generic Makers and the Abbreviated-New-Drug-Application (ANDA) Process

Generic drugs are versions of brand-name prescription drugs that typically contain the same active ingredients but not necessarily the same inactive ingredients as the brand-name original. *See United States v. Generix Drug Corp.*, 460 U.S. 453, 454-55 (1980); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1062 (D.C. Cir. 1998). Before 1984, a company that wished to make a generic version of an FDA-approved brand-name drug ("a generic maker") had to file another NDA. Preparation of the second NDA was as time-consuming and costly as the original, because the applicant had to include new studies showing the drug's safety and effectiveness. *See Mova*, 140 F.3d at 1063. In 1984, however, Congress enacted the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act, which simplified the procedure for obtaining approval of generic drugs. *See* Pub. L. No. 98-417, 98 Stat. 1585 (1984), codified at 21 U.S.C. § 355 and 25 U.S.C. §§ 156 and 271(e).

The Hatch-Waxman Act represented Congress's efforts to strike a compromise between the competing interests of pioneer pharmaceutical companies and generic manufacturers. As Chief Judge (then Judge) Edwards of the Court of Appeals for this Circuit explained, the Hatch-Waxman Act "emerged from Congress' efforts to balance two conflicting policy objectives: to induce name-brand pharmaceutical firms to make the investments necessary to research and develop new drug products, while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market." *Abbott Labs. v. Young*, 920 F.2d 984, 991 (D.C. Cir. 1990) (Edwards, J.,

dissenting on other grounds) (citations omitted), *cert. denied*, 402 U.S. 819 (1991). To this end, Title I of the Act aimed "to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962." H.R. Rep. No. 857 (Part I), 98th Cong., 2d Sess. at 14 (1984). Title II of the Act, by contrast, favored the interests of pioneer makers by granting patent-term extensions and guaranteeing market exclusivity for innovative drug products. *See id.* at 15.

Under the Hatch-Waxman Act, Congress continues to require the pioneer maker to file an NDA, complete with safety and effectiveness data. Subsequent applicants who wish to manufacture generic versions of the original drug, however, are required to file only an Abbreviated New Drug Application ("ANDA"). *See* 21 U.S.C. § 355(j). Unlike the stringent requirements for an NDA, an ANDA applicant need not show independent evidence of the safety and efficacy of its generic drug, but instead can rely on the FDA's previous determination that the drug is safe and effective. *See* 21 U.S.C. § 355(j); 21 C.F.R. § 314.94(a)(3); *Mead Johnson Pharm. Group v. Bowen*, 838 F.2d 1332, 1333 (D.C. Cir. 1988). The ANDA innovation thus allows manufacturers to market generic copies of pioneer drugs without repeating the expensive and lengthy clinical trials otherwise required by federal law. For this reason, among others, generic drugs are generally much cheaper to the consumer than brand-name drugs. *See Ben Venue Labs., Inc. v. Novartis Pharm. Corp.*, 10 F. Supp.2d 446, 449 (D.N.J. 1998); *see also Generix Drug Corp.*, 460 U.S. at 455 n.1.

To receive approval of its ANDA, an applicant must show that its generic drug is "bioequivalent" to the listed reference drug. *See* 21 U.S.C. § 355(j)(4)(F). Bioequivalence refers to the rate at which, and the extent to which, the body

absorbs the active ingredient(s) in the drug. *See id.* § 355(j)(8)(A); 21 C.F.R. § 320.1(e). In this case, the reference drug is BuSpar®, the brand of buspirone marketed by Bristol. The applicant must also show that the generic drug has the same route of administration, strength, and dosage form as the reference drug. *See* 21 U.S.C. §§ 355(j)(2)(A)(iii), (j)(4)(D)(i)-(ii); *see also* 21 C.F.R. § 314.92(a)(1) (1999) (indicating the categories of drug products for which an ANDA may be filed).

In addition, when a generic maker files an ANDA seeking approval of a generic version of a drug that is listed in the Orange Book, the applicant must certify that any patent information listed in the Orange Book does not bar FDA approval of a generic version of the drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.94(a)(12). The Hatch-Waxman Act provides ANDA applicants with four certification options: (I) that no patent information on the drug product that is the subject of the ANDA has been submitted to the FDA; (II) that the patent has expired; (III) that the patent will expire on a stated date; or (IV) that the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA applicant seeks approval. *See* 21 U.S.C. §§ 355(j)(2)(A)(vii)(I) to (IV). The court will refer to these certification clauses as Paragraph I, II, III and IV certifications, respectively. In the case of a patent that has not yet expired (such as the '365 patent), the ANDA applicant's only certification options are Paragraph III or IV certifications. *See id.*

The Hatch-Waxman Act also permits ANDA applicants to avoid certifying to a method- of- use patent if they are not seeking approval for any of the uses claimed in the patent. In that circumstance, the Act requires the ANDA applicant to make a statement to the FDA that the existing method-of-use

patent does not relate to the use(s) for which the ANDA applicant seeks approval. *See* 21 U.S.C. § 355(j)(2)(A)(viii); 21 C.F.R. § 314.94(a)(12)(iii). This statement is known as a "Section viii Statement."

The timing of FDA approval of the ANDA depends in part on the type of certification. If the ANDA contains a Paragraph I or II certification, the FDA may approve the ANDA as soon as it is satisfied that the product is safe and effective. *See* 21 U.S.C. § 355(j)(5)(B)(i). If the ANDA contains a Paragraph III certification, the FDA cannot make the approval effective until the patent expires. *See* 21 U.S.C. § 355(j)(5)(B)(ii). If the ANDA contains a Paragraph IV certification, the date of approval is determined by a complicated statutory scheme under which the ANDA applicant must provide notice to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA refers. *See* 21 U.S.C. § 355(j)(2)(B)(i). This notice must include a detailed statement of the factual and legal basis for the ANDA applicant's assertion that the patent is not valid or will not be infringed by its generic product. *See id.*; 21 C.F.R. § 314.95.

A Paragraph IV certification has significant legal effects. *See Ben Venue Labs.*, 10 F. Supp.2d at 449. The patent law provides that submitting an application for an infringing product is itself an act of infringement. *See id.* (citing 35 U.S.C. § 271(e)(2)(A)). Thus, a Paragraph IV certification automatically creates a cause of action for patent infringement.[2] *See id.* Upon receiving notice of a Paragraph

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[2] Paragraph IV certifications have occasioned more than their fair share of legal disputes. *See, e.g., Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998). The D.C. Circuit has described Paragraph IV as "far from a model of legislative draftsmanship." *See id.*

IV certification, the patent holder has 45 days in which to file suit against the generic manufacturer. *See* 21 U.S.C. § 355(j)(5)(B)(iii).[3] If the patent-holder brings such an action, the FDA is prohibited from approving the generic maker's ANDA for a period of 30 months. *See id.* This 30-month stay allows the parties to litigate the patent infringement action in court. If the court hearing the infringement action decides the patent would be infringed by the product proposed in the ANDA, the FDA will not approve the ANDA until the patent expires. If, however, the court hearing the infringement action rules before the expiration of the 30-month period that the patent is invalid or not infringed, the FDA must approve the ANDA effective on the date of the court's decision. *See id.*

The statutory framework of the Hatch-Waxman Act creates the potential for costly patent litigation against the generic maker that files a Paragraph IV-certified ANDA. As an incentive to the first generic maker to expose itself to the risk of costly patent litigation, Hatch-Waxman provides that the first to file a Paragraph-IV certified ANDA ("the first filer") is eligible for a 180- day period of exclusivity ("the Exclusivity Incentive"). *See* 21 U.S.C. § 255(j)(5)(B)(iv), as amended by Pub. Law. No. 105-115, 111 Stat. 2296 (1997);

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at 1069. In other instances, district courts have described Paragraph IV's provisions as "very confusing and ambiguous" and "cumbersome." *See id.* (citing *Mova Pharm. Corp. v. Shalala*, 955 F. Supp. 128, 130 (D.D.C. 1997) and *Mylan Pharms., Inc. v. Sullivan*, No. 89-36-C(K), slip. op. at 6 (N.D. W.Va. May 5, 1989)).

[3] The statute also provides that during the 45-day period after the ANDA applicant gives notice of its Paragraph IV certification, "no action may be brought under section 2201 of Title 28 for a declaratory judgment with respect to the patent." *See* 21 U.S.C. § 355(j)(5)(B)(iii)(III).

*Mova v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998). That is, during those 180 days, the FDA will not approve any other ANDA for the same generic product. By its terms, the Exclusivity Incentive affords the first filer protection from competition from subsequent generic makers for 180 days beginning from the earlier of a commercial marketing or a court decision. *See* 21 U.S.C. § 355(j)(5)(B)(iv)(I), (II).

## III. FACTUAL BACKGROUND

At the center of this dispute is a white, ovoid-rectangular, scored tablet called BuSpar®. *See* Mem. of Bristol-Myers Squibb Co. in Opp'n to Pl.'s Request for a Prelim. Inj. ("Bristol Opp'n"), Ex. 9 at 12; Fed. Defs.' Mem. in Opp'n to Pl.'s Mot. for Prelim. Inj. ("FDA Opp'n") at 8. Since 1986, Bristol has sold BuSpar®--which contains the active ingredient buspirone--as a medication to treat patients suffering from generalized anxiety disorder. *See* Mot. for Prelim. Inj. at 1. In 1999, Bristol sold more than $600 million of BuSpar®. *See id.* According to Bristol, BuSpar« "is one of those rare successes that provide[s] profits to its developer's shareholders and fund[s] research and development of new drugs--most of which are never successfully brought to market." Bristol Opp'n at 6.

Bristol received a patent covering the administration of buspirone to treat anxiety disorders in 1980, and obtained FDA approval of BuSpar® in 1986. *See* Mot. for Prelim. Inj. at 1. In addition, Bristol received a two-year extension to its 17-year patent term to compensate for the delays in regulatory approval of BuSpar®. *See id.* More recently, Bristol extended its exclusive rights over buspirone for an additional six months under the pediatric exclusivity provisions of the FFDCA, 21 U.S.C. § 355a. *See id.*; FDA Opp'n at 9. Bristol's term of exclusivity, which was set to

expire at 11:59 p.m. on November 21, 2000, has enabled it to sell BuSpar® for almost fifteen years without any competition from generic buspirone makers. *See* Mot. for Prelim. Inj. at 1.

Mylan is the nation's largest generic drug manufacturer. *See* Bristol Opp'n at 1. On September 29, 1998, Mylan submitted an ANDA to the FDA for a generic version of buspirone tablets. *See* FDA Opp'n at 9. Mylan's ANDA contained a Paragraph III certification stating that it would not market its generic product until the expiration of Bristol's patent 4,182,763 ("the `763 patent"). *See id.* The FDA "tentatively approved" Mylan's ANDA, with final approval contingent only on the expiration of Bristol's exclusivity on November 22, 2000. *See id.*; Mot. for Prelim. Inj. at 2. Anticipating the expiration of Bristol's exclusivity, Mylan took the steps necessary to put its buspirone product on the market, even loading its trucks with generic buspirone tablets for shipment beginning at 12:00 a.m. on November 22, 2000. *See* Mot. for Prelim. Inj. at 2.

Only twelve hours before Bristol's exclusivity was to expire, however, the U.S. Patent and Trademark Office ("PTO") issued patent 6,150,365 ("the `365 patent") to Bristol,[4] which Bristol immediately delivered to the FDA for listing in the Orange Book. *See id.* at 2; FDA Opp'n at 9;

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[4] The `365 patent resulted from an application Bristol filed with the PTO on June 6, 2000. *See* Mot. for Prelim. Inj. at 2. Bristol was able to obtain expedited issuance of its patent by filing a "petition to make special," a PTO procedure initiated by a patent applicant who wishes to expedite consideration of a patent application. *See id.* Bristol represented to the Patent Office that "in order to maintain its product position in what becomes a highly competitive market, [Bristol] requires issuance of this patent *prior to November 22, 2000.*" Mot. for Prelim. Inj., Leff Decl., Ex. 1 at M156 (emphasis in original).

Bristol Opp'n at 14. Bristol also submitted a declaration to the FDA stating that the `365 patent "is a method-of-use patent covering, among other things, a method of using BuSpar® for all of its approved indications." *See* FDA Opp'n at 9 (citing Bristol Declaration dated Nov. 21, 2000, Ex. B).[5] Bristol's submission to the FDA contained all the information required by the FDA's regulations, including the patent number, date of expiration, type of patent, a declaration that the `365 patent "covers the formulation, composition and/or method of use of BuSpar®," and an identification of the approved BuSpar® uses that are covered by the patent. *See* Bristol Opp'n at 14. As a result of the FDA's receipt of the `365 patent and accompanying declaration, the FDA did not give final approval to Mylan's ANDA (or to any other ANDAs) for generic buspirone tablets. *See* FDA Opp'n at 9-10.

The FDA's listing sparked a flurry of activity among Bristol, Mylan and other companies seeking to market a generic version of buspirone. On November 21, 2000, Bristol issued a press release regarding the `365 patent. *See* Bristol Press Release dated Nov. 21, 2000 (FDA Opp'n, Ex. C). As described in Bristol's press release, the `365 patent covers "a method of use of a metabolite produced by the administration of [buspirone]."[6] *Id.* Shortly after the FDA received the `365

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[5] The sole claim in the `365 patent covered:

> A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non- toxic anxiolytic dose of [6-hydrox-busprione] or pharmaceutically acceptable acid addition salt or hydrate thereof.

Mot. for Prelim. Inj., Ex. 3 at Col. 16, lines 27-32.

[6] A "metabolite" is a new molecule that is created after an existing pharmaceutical agent breaks down in the body. *See* Mot. for

patent, Mylan and Danbury Pharmacal, Inc. ("Danbury"), another company with a pending ANDA for buspirone, provided copies of the press release to the FDA. The FDA also received correspondence from Danbury, in which Danbury argued that under the Federal Circuit's ruling in *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997), a patent for a metabolite could not "claim a listed drug" within the meaning of the statute. *See* FDA Opp'n at 11 (citing Danbury Correspondence to FDA dated Nov. 24 & 27, 2000, Ex. B). In addition, on November 22, 2000, Mylan filed a Section viii Statement with the FDA stating that the labeling of its drug in the ANDA did not claim the method-of-use covered by the `365 patent.[7] *See* FDA Opp'n at 10 (citing Mylan Correspondence to FDA dated Nov. 22, 2000, Ex. D). Mylan requested that the FDA accept its Section viii Statement and approve its ANDA immediately. *See* Mot. for Prelim. Inj. at 9.

In light of these submissions, and faced with contradictory information about the `365 patent, the FDA

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Prelim. Inj. at 5. The chemical name for the active metabolite of buspirone is 6-Hydroxy-8-[4-[4-(2-pyrimindinyl)-piperazinyl]-butyl]-8-azaspiro[4.5]-7,9-dione. *See id.* For convenience, the court will refer to the metabolite by its internal BMS designation, BMY 28674. *See id.*

[7] Mylan's Section viii Statement stated as follows:

> With respect to the listed drug referred to in our [ANDA] for which information was filed [by Bristol] under subsection (b) or (c) for [the `365] patent, Mylan states that its labeling does not claim such a method of use.

Mot. for Prelim. Inj. at 9 (citing Leff Decl., Ex. 6). Mylan argues that it was "compelled" to make its Section viii Statement because, among other things, the `365 patent makes clear that it does not claim any of the currently approved methods of use of BuSpar®. *See* Mot. for Prelim. Inj. at 9.

requested additional input from Mylan, Danbury, and Bristol. *See* FDA Opp'n at 11. According to the FDA, it read the Bristol press release as suggesting that the `365 patent covered a metabolite of buspirone. *See id.* At the same time, the Federal Circuit's *Hoechst- Roussel* decision suggested to the FDA that patents for a drug's metabolites do not "claim" the listed drug itself. *See id.* The FDA therefore turned to Bristol for clarification as to whether the patent claimed only a metabolite of buspirone. Specifically, in a letter dated November 30, 2000, the FDA asked Bristol to provide "a declaration that the `365 patent issued by the PTO on November 21, 2000 contains a claim for an approved use of buspirone hydrochloride [the approved drug] that is separate from the claim for 6-hydroxy-buspirone [the metabolite] described in the November 21, 2000, Bristol-Myers Squibb press release." *See id.* at 11-12 (citing FDA Letter to Bristol dated Nov. 30, 2000, Ex. F). The FDA also asked Mylan and Danbury to submit additional legal analysis "to help the agency determine the impact of this Federal Circuit opinion [*Hoechst-Roussel*] on the patent listing process." *See* FDA Opp'n at 12.

The FDA requested this additional input from the parties on November 30, 2000. That same day, without responding to the FDA's request, both Mylan and Danbury filed suit in federal court. Mylan filed the instant action, naming both the FDA and Bristol as defendants. Danbury filed suit in the U.S. District Court for the District of Maryland, naming FDA Commissioner Jane Henney as the sole defendant. In both suits, the plaintiffs requested preliminary injunctive relief that would prevent the listing of the `365 patent and require the FDA to approve their buspirone ANDAs immediately. (The Maryland litigation is discussed in greater length below).

On December 4, 2000, Bristol submitted the clarification that the FDA had requested four days earlier. *See* Second Bristol Decl., dated Dec. 4, 2000 (FDA Opp'n, Ex. I). In its clarification, Bristol declared that the sole claim of the `365 patent was:

> a method for ameliorating an undesirable anxiety state comprising the direct administration of 6-hydrox-busprione [the metabolite] or oral administration of a prodrug[8] [buspirone] of 6-hydrox-busprione such as buspirone hydrochloride to provide an effective but non-toxic anxiolytic dose of 6-hydrox-busprione.

*Id.* Bristol also explained that the Bristol press release that Mylan and Danbury had provided to the FDA was "a short-hand, layperson's description of the patent." *See* Bristol Opp'n at 15. Finally, in a letter accompanying the declaration, Bristol reiterated that "the `365 patent does not simply claim a method of using [the metabolite], but also claims a method of using [buspirone itself]." *Id.* (Dec. 4, 2000 Letter) at 2.

Based on Bristol's clarification, and "consistent with [the FDA's] long-standing policy of accepting at face value the accuracy of such patent declarations, [the] FDA concluded that the Federal Circuit's ruling in *Hoechst-Roussel* was inapplicable because the `365 patent did not solely claim a metabolite." FDA Opp'n at 13. For this

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[8] A prodrug is a drug that converts *in vivo* to a patented form of drug, *see Zenith Labs., Inc. v. Bristol-Myers Squibb, Co.*, 1992 WL 171910, *25 (D.N.J. 1992), or as Mylan explains, "it is a drug which is metabolized into the metabolite," *see* Pl.'s Reply at 11 n.9. Thus, buspirone is a prodrug of BMY 28674. *See id.*

reason, the FDA informed Bristol that the clarification had "adequately responded" to the agency's concerns, and that the `365 patent would therefore be deemed to have been listed in the Orange Book on November 21, 2000. *See id.* (citing FDA Letter to Bristol dated Dec. 6, 2000, Ex. J).

## IV. THE MARYLAND LITIGATION

On November 30, 2000, the very day that Mylan instituted litigation in this court, two other generic drug companies, Watson Pharmaceuticals and Danbury Pharmacal (hereinafter "Danbury")[9] filed suit in the U.S. District Court for the District of Maryland. Like Mylan, Danbury sought an injunction ordering the de-listing of Bristol's `365 patent from the Orange Book. On January 18, 2001, U.S. District Judge Frederic N. Smalkin issued a Memorandum Opinion denying the plaintiffs' request for preliminary injunctive relief. *See Watson Pharm., Inc. and Danbury Pharmacal, Inc. v. Henney*, Civil Action No. 00-3516, (D. Md. Jan. 17, 2001). In his Opinion, Judge Smalkin described Danbury's suit as, "at base, a quest for judicial review of a federal agency's final decision" under the Administrative Procedure Act ("APA"), 5 U.S.C. § 706. *See id.* at 4. It is, of course, well-established that agency determinations are entitled to deference under *Chevron U.S.A., Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984). Noting that the FDA plays a limited, "ministerial" role in the patent fights between patent holders and generic makers, and in light of the traditional deference accorded to agency determinations, Judge Smalkin ruled that it was "not the business of the FDA

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[9] Danbury Pharmacal, Inc. is a wholly owned subsidiary of Schein Pharmaceutical, Inc., which, in turn, is a wholly owned subsidiary of Watson Pharmaceuticals, Inc. *See Watson v. Henney*, Civil Action No. 00-3516 (D. Md.) (FNS), Compl. ¶ 6.

or of this Court in an APA review, to adjudicate the *merits* of the scope and/or validity of the claims covered by the `365 patent." *See id.* at 5 (emphasis in original). Accordingly, Judge Smalkin ruled that since the FDA's action was not "unreasonable, arbitrary, or capricious," the federal defendants were entitled to summary judgment on the merits. *See id.*

Because Bristol and the FDA have urged this court to adopt Judge Smalkin's reasoning, it is worth examining how this case differs from the Maryland litigation. First, Danbury did not sue Bristol. *See id.* at 7. In fact, although Bristol ultimately intervened as a defendant in the Maryland litigation, Danbury did not request any relief against Bristol. *See id.* Second, Danbury did not raise the issue of whether Bristol's `365 patent was one as to which a claim of patent infringement could reasonably be asserted. *See id.* Finally, Danbury did not submit a Section viii Statement to the FDA, and therefore did not argue, as did Mylan, that the FDA was required to accept its Section viii Statement. *See id.*

The FDA has endorsed Judge Smalkin's ruling, reiterating to this court that its role in listing patents is "purely ministerial" and that it "does not have the expertise nor the resources to resolve complex patent coverage issues." *See* FDA Opp'n at 19 (citing 54 Fed. Reg. 28872, 28909-10 (July 10, 1989)). For this reason, among others, the FDA argues that Mylan's remedy is not to sue the agency, but rather to ask the court hearing its patent claims to modify the presumptive 30-month statutory stay on FDA approval of Mylan's ANDA. *See* FDA Opp'n at 23; *see also* 21 U.S.C. § 355(j)(5)(B)(iii) (providing that 30-month stay may be modified by the court hearing the patent litigation).

Mylan responds that it is not asking the FDA to perform

anything *but* a ministerial act. As Mylan explained at oral argument, the FDA is "an important player here because if we were to sue Bristol alone and not the FDA and there were to be an order directed to Bristol asking Bristol to request [that] the patent be delisted from the Orange Book, we might still need relief against the FDA if the FDA, for whatever reason, declined to do so." *See* Tr. of Oral Argument dated Jan. 24, 2001 ("Tr.") at 8. In other words, Mylan has placed the "substantive burden" in this matter on Bristol. *See id.* at 7. Indeed, with the exception of the Section-viii-Statement issue, Mylan is challenging only Bristol's actions, not the FDA's. *See* Pl.'s Reply Mem. In Support of Mot. for Prelim. Inj. ("Pl.'s Reply") at 3-4. Specifically, Mylan asks the court to declare that *Bristol* improperly submitted the `365 patent to the FDA for inclusion in the Orange Book. *See id.* at 4. In this way, Mylan has cleverly avoided the problem that Danbury faced in its suit, namely that the FDA's decision to list the `365 patent was entitled to a presumption of validity under *Chevron* and its progeny.

## V. DISCUSSION

### A. Subject-Matter Jurisdiction

Before proceeding to the preliminary-injunction analysis, the court must address Bristol's argument that Mylan does not identify any recognized cause of action in support of its request for relief. *See* Bristol Opp'n at 22-23. According to Bristol, Mylan's lawsuit is not the appropriate vehicle for challenging Bristol's submission of the `365 patent for inclusion in the Orange Book. *See id.* This is so, Bristol argues, because Mylan seeks to enforce the FFDCA--a statute which by its terms does not allow for a private right of action. *See id.* at 22; *see also* 21 U.S.C. § 337(a) ("proceedings for the enforcement, or to restrain

violations, of the [statute] shall be by and in the name of the United States"). Indeed, as Bristol points out, "every federal court that has addressed the issue has held that the FFDCA does not create a private right of action." *See* Bristol Opp'n at 22 (citing *Eli Lilly & Co. v. Roussel Corp.*, 23 F. Supp.2d 460, 476 (D.N.J. 1998)); *see also In re Orthopedic Bone Screw Prods. Liab. Litig.*, 193 F.3d 781, 788 (3d Cir. 1999); *PDK Labs., Inc. v. Friedlander*, 103 F.3d 1105, 1113 (2d Cir. 1997); *Bailey v. Johnson*, 48 F.3d 965, 966-68 (6th Cir. 1995); *Mylan Labs., Inc. v. Matkari*, 7 F.3d 1130, 1139 (4th Cir. 1993), *cert. denied*, 510 U.S. 1097 (1994); *Rodriguez v. SK & F Co.*, 833 F.2d 8, 9 (1st Cir. 1987) (per curiam). For this reason, Bristol urges the court to hold that Mylan has failed to state a claim upon which relief can be granted. *See* Bristol Opp'n at 22.

Mylan, however, does not seek to enforce the FFDCA against Bristol. *See* Pl.'s Reply at 4. Rather, Mylan asks the court to declare that Bristol improperly submitted the `365 patent to the FDA for inclusion in the Orange Book because that patent did not meet 21 U.S.C. § 355(c)(2)'s requirements for such a listing. *See id.* Mylan also asks that the court, upon making this determination, order Bristol to withdraw its submission of the `365 patent, and instruct the FDA to perform the "ministerial" task of de-listing the `365 patent from the Orange Book. *See id.* Mylan contends--and the court agrees--that these requests are proper under the Declaratory Judgment Act, 28 U.S.C. § 2201. *See id.* at 4-5.

### 1. The Declaratory Judgment Act

The Declaratory Judgment Act permits federal courts to "declare the rights and other legal relations" of parties to "a case or actual controversy." *See* 28 U.S.C. § 2201. The Act does not enlarge the jurisdiction of federal courts beyond

what is constitutionally permissible, but widens the range of remedies that federal courts have at their disposal. *See Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 667, 771-72 (1950). The sole requirement for jurisdiction under the Act is that the conflict be "real and immediate, *i.e.*, that there be a true, actual `controversy.'" *See Arrowhead Indus. Water, Inc. v. Ecolochem, Inc.*, 846 F.2d 731, 735 (Fed. Cir. 1988). The "actual controversy" requirement, in turn, mirrors the "case or controversy" requirement of Article III of the United States Constitution. *See Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 239- 41 (1937). Thus, the Declaratory Judgment Act requires no more rigorous a showing of justiciability than the Constitution does.[10]

Several courts have held that an action to delist a patent

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[10] Declaratory relief is "indisputably appropriate" in patent cases. *Societe de Conditionnement en Aluminium v. Hunter Eng'g Co., Inc.*, 655 F.2d 938, 943 (9th Cir. 1981) (citing *Hanes Corp. v. Millard*, 531 F.2d 585, 592 (D.C. Cir. 1972)). As the Second Circuit has explained:

> the availability of declaratory relief has destroyed the "racket" by which patentees gained manifold advantages by the device of threatening alleged infringers or their customers with lawsuits which might never be brought or, if brought, could always be dismissed without prejudice, without the possibility of such persons taking steps to ascertain the validity of the patentee's claims.... Because of the public policy in breaking this "racket," and in preventing an invalid patent from remaining in the art "as a scarecrow"... the declaratory remedy should be construed with liberality in the patent field as in general.

*Wembley, Inc. v. Superba Cravats, Inc.*, 315 F.2d 87, 89 (2d Cir. 1963) (internal citations omitted). Thus, the Declaratory Judgment Act serves the policies underlying patent law by allowing litigants to test the validity and infringement of patents that are being used as what Judge Learned Hand called "scarecrows." *See Arrowhead*, 846 F.2d at 735 n. 4 (citing *Bresnick v. United States Vitamin Corp.*, 139 F.2d 239, 242 (2d Cir. 1943)).

from the Orange Book may be brought under the Declaratory Judgment Act. For example, in *Ben Venue Laboratories v. Novartis Pharmaceutical Corp.*, 10 F. Supp.2d 446, 451-52 (D.N.J. 1998), the defendant was the pioneer maker of Aredia, a drug designed to treat bone loss and complications from cancer. *See id.* at 450. In the Orange Book, Aredia was listed with U.S. Patent No. 4,711,880 ("the `880 patent"). *See id.* Ben Venue, a generic maker, had filed an ANDA to manufacture and sell a generic version of Aredia. Before addressing the merits of the parties' claims, the court determined that the plaintiff was entitled to request declaratory relief against an Orange-Book listing, even during the 45-day moratorium on declaratory judgments for infringement. *See id.* Indeed, the court expressly held that while a challenge to the appropriateness of an Orange Book listing may be raised as a counterclaim in a patent infringement suit, this "is not the only way such a challenge can be brought. The Court sees no reason why a party must wait until it is sued for patent infringement to raise the issue of an improper Orange Book listing." *See id.* at 452 n. 4.[11]

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[11] The FDA argues that the Hatch-Waxman Act "provides that interested generic and innovator firms [must] resolve any patent disputes concerning a drug, including whether a patent `claims' the approved drug product, in private litigation." FDA Opp'n at 18 (citing 21 U.S.C. § 355(j)(2)(A)(vii)(IV); § 255(j)(2)(B); and § 255(j)(5)(B)(iii)). In *Ben Venue*, however, the court held that declaratory judgment suits brought by potential generic competitors concerning allegedly inappropriate "Orange Book" listings can be initiated outside the context of the Hatch-Waxman Act. *See Ben Venue Labs.*, 10 F. Supp.2d at 451-52; *see also* Gregory J. Glover, *Regulatory Concerns & Market Exclusivity*, 1175 PLI/CORP 629, 646 (2000) (stating that if "other courts" adopt the view of the Ben Venue court, generic competitors will be able to raise Orange Book listings substantially in advance of having to make patent certifications in generic applications).

Bristol attempts to distinguish *Ben Venue* on the grounds that in that case, the patent holder had asserted a claim for infringement, whereas in the instant matter, there is neither a claim of patent infringement nor a claim for a declaration of non-infringement, invalidity, or unenforceability. *See* Bristol Supp. Brief at 2 n.2. Bristol fails to note, however, that Ben Venue did not bring a declaratory action for non-infringement but "only raised the propriety of the listing of the [defendant's patent] under the food and drug laws." *See Ben Venue Labs.*, 10 F. Supp.2d at 451. As the court explained: "Ben Venue's lawsuit did not explicitly challenge the validity of the patent or state that its product was noninfringing. Instead, Ben Venue asserted that the `880 Patent does not `claim' Aredia and that the patent is therefore improperly listed in the Orange Book." *Id.* at 450.

Bristol also fails to note another critical factor in the *Ben Venue* decision, namely that the defendant did not file a patent infringement suit against Ben Venue until after Ben Venue had filed its declaratory judgment action. *See id.* In other words, as in the present matter, when Ben Venue brought its declaratory judgment action, the defendant had not yet filed its suit for patent infringement. *See id.* Finally, although Ben Venue later amended its pleadings to add a claim for declaratory judgment of non-infringement, the court specifically held that the original declaratory- judgment claim was not jurisdictionally barred. *See id.* at 452. For these reasons, Bristol's efforts to distinguish *Ben Venue* are unavailing.

Similarly, in *Zenith Laboratories, Inc. v. Abbott Laboratories, Inc.*, the plaintiff ANDA applicant sought a declaration that the defendant NDA-holder had improperly listed its patents in the Orange Book. *See Zenith Labs.*, 1996 U.S. Dist. LEXIS 22567, *20 (D.N.J. 1996). The defendant

moved to dismiss on the same ground advanced here by Bristol--that the plaintiff's action was an attempt to enforce the FFDCA and that the FFDCA does not provide a private cause of action. The Court denied the defendant's motion, stating that it " is not an action under the FFDCA plaintiff seeks to pursue but [rather an action] under the Declaratory Judgment and All Writs Acts and state law." *See id.* at 22.[12]

Bristol again attempts to distinguish *Zenith*, arguing that unlike Mylan, the generic maker- plaintiff in *Zenith* sought a declaratory judgment of non-infringement, invalidity or unenforceability. *See* Bristol Supp. Brief at 2 n.2. As Bristol states, "[w]e are not aware of a single case holding that an action to delist a patent from the Orange Book is properly grounded solely upon the [Declaratory Judgment Act] where there is neither a claim of patent infringement nor a claim for a declaration of non-infringement, invalidity or unenforceability." *Id.* Mylan responds that because there must be subject-matter jurisdiction over each claim in a lawsuit, the fact that there was also a claim for declaratory judgment of non-infringement in Zenith is irrelevant. *See* Pl.'s Supp. Reply Supp. Brief at 2 (citing *Mineba Co., Ltd. v. Papst*, 13 F. Supp.2d 35, 40 (D.D.C. 1998) (dismissing certain counts for lack of subject-matter jurisdiction while declining to dismiss other declaratory-judgment counts that "arise under" the patent laws)).

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[12] The *Zenith* court also noted that the Northern District of Illinois had entertained a request for a declaratory judgment against Abbott, found Abbott's listings to be improper, and ordered Abbott to remove those patents from the Orange Book. *See id.* at 22 n.2 (citing *Abbott Labs. v. Geneva Pharms.*, 1996 U.S. Dist. LEXIS 9762 (N.D. Ill. 1996)).

Bristol's efforts to distinguish *Zenith* and *Ben Venue* take aim at a more fundamental issue: whether there is an underlying basis for federal jurisdiction here beyond the Declaratory Judgment Act. As Bristol correctly noted at oral argument, the Declaratory Judgment Act, standing alone, does not confer jurisdiction on a federal court. *See* Tr. at 28; *see also Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 876, 878-79 (1950) (the "operation of the Declaratory Judgment Act is procedural only"); *Superlease Rent-A-Car, Inc. v. Budget Rent-A-Car of Md., Inc.*, 1989 WL 39393, *3 (D.D.C. 1989) (holding that because Declaratory Judgment Act provides no independent cause of action, the plaintiff must first assert an interest in itself which the law recognizes). Thus, independent of the applicability of cases like *Zenith* and *Ben Venue*, the court must determine whether it has subject-matter jurisdiction over Mylan's request for declaratory judgment.

The test for determining whether an actual controversy exists in a patent case has been phrased in many ways, depending on the facts of the particular case. *See Mineba Co., Ltd. v. Papst*, 13 F. Supp.2d at 39. In the classic patent declaratory judgment suit, the two core elements of the test are: (1) whether the defendant's acts create a "reasonable apprehension" on the part of the plaintiff that it will face an infringement suit or whether "the acts of the defendant indicate an intent to enforce its patent;" and (2) whether acts of the plaintiff might subject it or its customers to a suit for patent infringement. *See id.* (citations omitted); *see also DuPont Merck Pharm. Co. v. Bristol-Myers Squibb*, 62 F.3d 1397, 1401 (Fed. Cir. 1995).[13] Notably, there need not be an

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[13] Satisfaction of this two-part test is not a prerequisite to jurisdiction in every possible patent declaratory-judgment action. *See Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1470 (Fed. Cir. 1997).

express threat of infringement to establish an actual case or controversy. *See Goodyear Tire & Rubber Co. v. Releaseomers, Inc.*, 824 F.2d 953, 955-56 (Fed. Cir. 1987). As the Federal Circuit has held, such a requirement would defeat the purpose of the Declaratory Judgment Act, which in patent cases is to provide the allegedly infringing party relief from uncertainty and delay regarding its legal rights. *See id.* (citing Moore's Federal Practice ¶ 57.08[2] (1986)).

Mylan satisfies both elements of the test. First, Bristol's actions have created a reasonable apprehension in Mylan that it could face an infringement suit or that Bristol intends to enforce its patent. By listing the `365 patent in the Orange Book, Bristol represented that the patent satisfies the requirements of 21 U.S.C. § 355(c)(2). In other words, Bristol represented that the `365 patent is one "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale" of buspirone and that the `365 patent "claims a method of using" buspirone. *See* 21 U.S.C. § 355(c)(2); Decl. of Richard P. Ryan (FDA Opp'n , Ex. I). Moreover, in its Petition to Expedite Issuance of [the `365] Patent, Bristol represented to the PTO that "to maintain its product position in what becomes a highly competitive market, assignee requires issuance of this patent *prior to November 22, 2000*." Mot. for Prelim. Inj., Leff Decl., Ex. 1 at M156 (emphasis in original). The purpose of this representation (as characterized by Mylan) was to ensure that the `365 patent could be listed in the Orange Book before the expiration of Bristol's pediatric exclusivity and to permit

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"Indeed, the two elements merely assure that the declaratory plaintiff has enough interest in the subject matter of the suit and that the disagreement between the parties is real and immediate enough to fulfill the `actual controversy' requirement. *See id.*

Bristol to use the Hatch-Waxman Act's certification and lawsuit-filing procedures to block FDA approval of Mylan's ANDA. *See* Pl.'s Supp. Brief at 4. Finally, on November 27, 2000, Bristol's Senior Patent Counsel sent a letter to Mylan specifically calling attention to the `365 patent and giving Mylan directions on how to serve a Paragraph IV notice on Bristol with respect to that patent. *See id.*, Ex. B. Bristol's actions indicate that Mylan was in reasonable apprehension of being sued and that, by causing the `365 patent to be listed in the Orange Book, Bristol effectively blocked FDA approval of Mylan's ANDA. *See* Pl.'s Supp. Brief at 4.

With respect to the second requirement for a patent controversy, the Federal Circuit has held that a plaintiff "must be engaged in an actual making, selling, or using activity subject to an infringement charge or must have made meaningful preparation for such activity." *See Arrowhead*, 846 F.2d at 736. Mylan is in a position to begin marketing its generic product immediately upon FDA approval. Indeed, Mylan has already developed a generic equivalent of BuSpar®, filed an ANDA with respect to that product, obtained tentative FDA approval of its ANDA, and packed its buspirone product into trucks and onto the loading dock on November 21, 2000 in anticipation of final FDA approval. *See* Pl.'s Response at 4. Thus, not only did Mylan engage in potentially infringing activity, it was only twelve hours away from selling its product. *See id.* By contrast, courts have held that the more acute case-or-controversy problem arises when the plaintiff has not yet begun to manufacture, or make preparations to manufacture, the patented product. *See, e.g.*, *Societe de Conditionnement en Aluminium v. Hunter Eng'g Co., Inc.*, 655 F.2d 938, 944 (9th Cir. 1981). "In that situation, the plaintiff is asking the court to render an advisory opinion whether its product would be infringing a valid patent." *See id.* Mylan's substantial preparations for the

sale of its generic buspirone product demonstrate that it does not seek an advisory opinion.

### 2. Is This a "Patent Case"?

Notwithstanding the above discussion, Bristol argues that this two-part test does not apply because the instant matter is not a "patent case." *See* Bristol Supp. Brief at 2, 2 n.1. Indeed, Bristol argues that Mylan has simply fashioned this case as a "patent case" in an effort "to create the appearance of a justiciable case or controversy," when in fact "[t]his is an administrative law case in which Mylan challenges [Bristol's] submission to the FDA of information relating to the `365 patent and the FDA's decision to publish BMS's submission in the Orange Book and to withhold approval of Mylan's ANDA prior to the expiration of the waiting period imposed by Congress." *See* Bristol Supp. Brief at 3.

Bristol's contention that this is not a "patent case" implicitly challenges whether Mylan's case "arises under" the federal patent laws. Under 28 U.S.C. § 1338(a), "district courts shall have original jurisdiction of any civil action arising under any Act of Congress relating to patents...." *In Christianson v. Colt Indus. Operating Co.*, 486 U.S. 800, 808-809 (1988), the Supreme Court outlined the dimensions of section 1338(a):

> [Section] 1338(a) jurisdiction likewise extend[s] only to those cases in which a well- pleaded complaint establishes either that federal patent law creates the cause of action or that the plaintiff's right to relief necessarily depends on resolution of a substantial question of federal patent law, in that patent law is a necessary element of one of the well-pleaded claims.

*Id.* Thus, section 1338(a) gives district courts jurisdiction over causes of action created by federal law and causes of action whose resolution depends on a substantial question of federal patent law. *See id.*; *Additive Controls & Measurement Sys., Inc. v. Flowdata, Inc.*, 986 F.2d 476, 478 (Fed. Cir. 1993). The Federal Circuit recently stated that Christianson sets a "lenient standard" for jurisdiction under 28 U.S.C. § 1338(a). *See United States Valves, Inc. v. Dray*, 212 F.3d 1368, 1372 (Fed. Cir. 2000).

A purported declaratory judgment action must be analyzed pursuant to the well-pleaded complaint rule. *See, e.g., Speedco, Inc. v. Estes*, 853 F.2d 909, 912 (Fed. Cir. 1988). The well-pleaded complaint rule is applied "not to the declaratory judgment complaint, but to the action that the declaratory defendant would have brought." *Minebea Co. v. Papst*, 13 F. Supp.2d 35, 40 (D.D.C. 1998) (citations omitted). Here, the action that Bristol--the declaratory defendant--would have brought was a claim for infringement of the `365 patent. It would not have been, as Bristol contends, a suit by Bristol against Mylan to require listing of the `365 patent in the Orange Book. *See* Bristol Supp. Brief at 2. Because a claim for patent infringement "is clearly a claim which `arises under' the patent laws as contemplated by 28 U.S.C. § 1388(a)," the court has subject-matter jurisdiction over Mylan's claims against Bristol. *See Mineba*, 13 F. Supp.2d at 40; *see also* Mylan Supp. Reply Brief at 4-5 ("It would be hard to imagine an issue which depends more on a substantial question of federal patent law than whether the `365 patent covers ... BuSpar® and whether a claim for patent infringement could reasonably be asserted against that product").

Finding jurisdiction in this case is not inconsistent with *Speedco, Inc. v. Estes*, 853 F.2d 909 (Fed. Cir. 1988). In that

case, the court held that the declaratory defendant's hypothetical action would not "arise under" the federal patent law because the defendant did not have a colorable claim of ownership in the subject patent and therefore had no right to sue for patent infringement. *See id.* The declaratory defendant's only other possible claim was for breach of contract relating to a patent, which would not have required the declaratory defendant to plead patent validity as a necessary element of the complaint. *See id.* The court thus concluded that the declaratory plaintiff could not establish jurisdiction under the well-pleaded complaint rule. *See id.* By contrast, the action Bristol would have brought here was a claim for infringement of the `365 patent--clearly an action "arising under" the patent laws for the purpose of federal jurisdiction.

Based on this analysis, the court concludes that Mylan has stated a recognized cause of action in support of its request for relief, and that this court has subject-matter jurisdiction to hear this cause of action. In addition, Mylan has demonstrated that this matter does present a case or controversy such that this court is not in the position of rendering an advisory opinion. *See, e.g., Flast v. Cohen*, 392 U.S. 83, 96-97 (1968) (discussing origins of prohibition on advisory opinions). Accordingly, the court will proceed to the preliminary-injunction analysis.

### B. Preliminary Injunction Standard

A preliminary injunction is an extraordinary form of judicial relief. *See Moore v. Summers*, 113 F. Supp.2d 5, 17 (D.D.C. 2000). Although the issuance or denial of a preliminary injunction rests in the sound discretion of the trial court, it is not a form of relief granted lightly. *See Ambach v. Bell*, 686 F.2d 974, 979 (D.C. Cir. 1982).

Traditionally, courts must examine four factors: (1) whether there is a substantial likelihood that the plaintiff will succeed on the merits; (2) whether the plaintiff will be irreparably injured if an injunction is not granted; (3) whether an injunction will substantially injure the non-moving party; and (4) whether the public interest will be furthered by the injunction. *See* Fed. R. Civ. P. 65; *Serono Labs. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C. Cir. 1998); *Washington Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 843 (D.C. Cir. 1977). Courts do not consider these factors in isolation from one another, and no one factor is necessarily dispositive. *See CityFed Fin. Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746 (D.C. Cir. 1995). Rather, the factors "interrelate on a sliding scale and must be balanced against each other." *Davenport v. Int'l Bhd. of Teamsters*, 166 F.3d 356, 361 (D.C. Cir. 1999) (citing *Serono Labs.*, 158 F.3d at 1317-18).

If the plaintiff makes a particularly weak showing on one factor, however, the other factors may not be enough to compensate. *See Taylor v. Resolution Trust Corp.*, 56 F.3d 1497, 1506 (D.C. Cir. 1995), *amended on other grounds on reh'g*, 66 F.3d 1226 (D.C. Cir. 1995). Indeed, in this Circuit, the first factor--likelihood of success on the merits--is the most important one, for absent such an indication, "it would take a very strong showing with respect to the other preliminary injunction factors to turn the tide in plaintiffs' favor." *See Davenport*, 166 F.3d at 366 (citing *Murrow Furniture Galleries v. Thomasville Furniture Indus.*, 889 F.2d 524, 527 (4th Cir. 1989)).

In this case, Mylan faces an additional hurdle because it seeks a mandatory injunction as opposed to a prohibitive injunction. *See Mylan Pharms., Inc. v. Shalala*, 81 F. Supp.2d 30, 36 (D.D.C. 2000); *Mylan Pharms, Inc. v.*

*Henney*, 94 F. Supp. 2d 36, 58 (D.D.C. 2000) (Urbina, J.). That is, Mylan seeks a preliminary injunction not to maintain the status quo while this matter can be resolved on the merits, but rather to alter the status quo by requiring the FDA to approve its ANDA. In this Circuit, "the power to issue a preliminary injunction, especially a mandatory one, should be sparingly exercised." *See Mylan*, 94 F. Supp. 2d at 58 (citing *Dorfmann v. Boozer*, 414 F.2d 1168, 1173 (D.C. Cir. 1969) (internal quotations and citations omitted)); *see also Columbia Hosp. for Women Found., Inc. v. Bank of Tokyo-Mitsubishi, Inc.*, 15 F. Supp. 2d 1, 4 (D.D.C. 1997), *aff'd*, 159 F.3d 636 (D.C. Cir. 1998).

### C. Preliminary-Injunction Analysis

#### 1. Prong 1: Whether Mylan is Likely to Succeed on the Merits

Under the first prong of the preliminary-injunction analysis, the court must consider whether the movant is likely to succeed on the merits. Mylan states that it is entitled to immediate FDA approval of its ANDA, and therefore is likely to succeed on the merits, for two "separate and independently sufficient" reasons. *See* Mot. for Prelim. Inj. at 3. First, Mylan argues that the `365 patent does not meet the two statutory listing requirements of 21 U.S.C. §§ 355(b)(1) and (c)(2). *See id.* Second, Mylan argues that "even if the `365 patent were properly listed, the FDA violated the applicable statute and its long-standing practice by refusing to accept Mylan's [Section viii Statement] that the `365 patent `does not claim a use for which [Mylan] is seeking approval.'" *Id.* Because the court finds Mylan's

Section-viii-Statement argument unpersuasive,[14] the court will focus primarily on Mylan's contention that Bristol's `365 patent does not meet the two statutory listing requirements of 21 U.S.C. §§ 355 (b)(1) and (c)(2).

Mylan argues that the `365 patent has been improperly listed because: (1) the patent does not meet the statutory listing requirement that it "claim the drug" or "a method of using" the drug for which Bristol had obtained FDA approval; and (2) the patent does not meet the statutory requirement that "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the [approved] drug." *See* Mot. for Prelim. Inj. at 3 (citing 21 U.S.C. § 355(b)(1)).

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[14] In brief, Mylan's Section-viii-Statement argument is as follows: Bristol submitted a statement to the FDA to the effect that the `365 patent covers all approved uses for BuSpar(R). Mylan submitted a Section viii Statement to the FDA certifying that its labeling did not claim a method of use covered by the `365 patent. Mylan argues that the FDA was required to accept its Section viii Statement, which was required and authorized by statute, and reject Bristol's statement, which was not required by statute, and therefore was "gratuitous." *See* Mot. for Prelim. Inj. at 28. In other words, Mylan argues that the FDA should defer to its interpretation of the scope of the `365 patent and not to Bristol's submission identifying the protected use.

For the purposes of the present motion, the court does not find it necessary to engage in a lengthy discussion of Mylan's Section-viii-Statement argument, particularly since Mylan has demonstrated a substantial likelihood of success on the merits of its other two arguments. The court does note, however, that Bristol has offered a persuasive characterization of Mylan's argument: "In effect, Mylan argues that it is the final arbiter of whether or not a method of use patent covers the use for which it is seeking approval, and that the FDA was bound to accept Mylan's judgment on that question." Bristol Opp'n at 20.

With respect to the first of these listing requirements, Mylan argues that the `365 patent claims a method of using a buspirone metabolite (BMY 28674). *See id.* The patent does not, contends Mylan, claim buspirone--the approved drug--or a method of using buspirone. *See id.* As for the second listing requirement, Mylan contends that Bristol's representation that a claim of patent infringement could reasonably be asserted against an unauthorized user, maker or seller of the approved drug was false because "the `365 patent makes quite plain, by its express language, that to the extent that the `systemic administration' of BMY 28674 can be accomplished by administration of buspirone itself, the claimed invention includes administration of buspirone only `in such a manner that the metabolic production of BMY 28674 is favored.'" *See id.* at 6 (citing `365 patent, col. 12, lines 14-15, Leff Decl. Ex. 3).

The court will address in turn the two statutory listing requirements of 21 U.S.C. § 355(c) and Mylan's arguments with respect to each.

**a. The `365 Patent Does Not "Claim" a Method of Using BuSpar®**

With respect to the first statutory listing requirement--that the `365 patent claim a method of using the approved drug--Mylan relies on Federal Circuit precedent to suggest that the `365 patent does not claim a method of using BuSpar®. Specifically, Mylan argues that Bristol's filing of the `365 patent violated the Federal Circuit's holding in *Hoechst-Roussel Pharms., Inc. v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997) ("*Hoechst*"). Because *Hoechst* dealt with a different provision of the Hatch-Waxman Act than the provision at issue here, the court must first determine whether *Hoechst* is applicable to the case at bar.

In *Hoechst*, the Federal Circuit considered whether a drug manufacturer could obtain a patent term extension under 35 U.S.C. § 156 of the Hatch-Waxman Act ("Section 156"). Section 156 provides that:

> (a) the term of a patent *which claims a product, a method of using a product*, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent if...
>
> * * *
>
> (4) the product has been subject to a regulatory review period before its commercial marketing or use.

35 U.S.C. § 156(a) (emphasis added). Bristol submitted the `365 patent to the FDA for listing in the Orange Book pursuant to 21 U.S.C. § 355(c)(2) ("Section 355"). Section 355 requires, among other things, that the patent "claim a method of using" the approved drug. See 21 U.S.C. §§ 355(c)(2). Mylan argues that because Section 156 and Section 355 both require that a patent "claim a method" of use, the Federal Circuit's holding in Hoechst should apply to the instant matter.

A summary of the *Hoechst* decision may help frame the issues that Mylan has raised. In 1990, Warner-Lambert Co. ("Warner") submitted an NDA to the FDA for approval of COGNEX® to treat Alzheimer's disease. *See Hoechst*, 109 F.3d at 757. The active ingredient in COGNEX was tacrine hydrochloride. *See id.* In 1993, the FDA granted Warner approval to market COGNEX®, whereupon Hoechst sued Warner for infringement of Hoechst's `286 patent, which had

issued in 1986. *See id.* Hoechst's `286 patent did not claim tacrine hydrochloride itself; rather, it disclosed and claimed both the compound 1-hydroxy-tacrine and a method of treating patients in need of memory enhancement by administering an effective amount of 1- hydrox-tacrine. *See id.* In addition, and of moment to Mylan's claim, tacrine hydrochloride metabolized into 1-hydroxy-tacrine and other compounds after ingestion. *See id.*

While in litigation over the alleged infringement of the `286 patent, Hoechst applied for an extension of the term of its patent pursuant to Section 156, based on the Warner-initiated regulatory review period of COGNEX®. *See id.* Hoechst argued that it was entitled to this extension because the administration of the approved drug product resulted in the production in the body of the metabolite, and that administration of the drug product itself therefore infringed the patent claim. In 1995, the Commissioner of Patents and Trademarks denied Hoechst's application for an extension. The Commissioner decided that, among other things, Hoechst's `286 patent did not "claim" either tacrine hydrochloride or a method of using that product. *See id.* at 758.

On appeal to the Federal Circuit, Hoechst argued that a patent "claims" an FDA- approved product within the meaning of Section 156 if the FDA-approved product would infringe a claim of that patent. *See Hoechst*, 109 F.3d at 758. Because use of tacrine hydrochloride allegedly infringed its claim to a method of using 1-hydroxy-tacrine, Hoechst argued that the `286 patent "claimed" a method of using tacrine hydrochloride. *See id.* The Federal Circuit sided with the Commissioner, holding that Hoechst's `286 patent claimed neither tacrine hydrochloride nor a method of using that product. *See id.* at 761. Mylan argues here that just as the

metabolite patent in *Hoechst* did not "claim" the drug product or the method of its use, so too Bristol's `365 patent does not "claim" a method of using BuSpar®. *See* Mot. for Prelim. Inj. at 18. According to Mylan, Hoechst demonstrates that the `365 patent is not properly listed in the Orange Book because it *claims* neither the approved drug nor a method of administering it. *See id.*

Bristol responds that Mylan's reliance on the *Hoechst* case is misplaced because *Hoechst* involved a different statute (Section 156) and thus a different issue (whether a drug manufacturer could obtain a patent term under section 156). *See* Bristol Opp'n at 26. In fact, Section 355 and Section 156 are, in a sense, competing provisions of the same act. Section 156 (which Judge Smalkin described as the "carrot" portion of the Hatch-Waxman Act) provides patent holders with an increased incentive for drug research and innovation by restoring some of the time lost in regulatory review to their patent term. *See* H.R. Rep. No. 98-857, pt. I at 15 (1984). Section 355 relates to the expedited approval for generic equivalents (and forms part of what Judge Smalkin described as the "stick" portion of the Act).

In *Hoechst*, the primary issue facing the Court was the meaning of the statutory term "claims." *See Hoechst*, 109 F.3d at 758. Noting that statutory words must be given their ordinary meaning unless "otherwise defined" by Congress, the *Hoechst* Court found nothing in the legislative history of Section 156 to suggest that Congress had "otherwise defined" the word "claims." *See id.* at 759-60. Quite to the contrary, the court read the legislative history of Section 156 to suggest that Congress had "deliberately chosen the term `claims' because [the word] already had a well-known meaning and usage in patent law. *See id.* at 760. Based on its interpretation of the term "claims," the Federal Circuit

concluded that there was a difference between claiming the chemically distinct product and the method of using the product, and claiming the active ingredient that has received FDA approval, or a method of using that ingredient.

Although Section 156 implements different policies than Section 355, this court has not found, and Bristol has not cited, anything from the legislative history of the Hatch-Waxman Act to suggest that the plain language of Section 156 and the plain language of Section 355 should be interpreted differently. Nor has Bristol suggested that the word "claims," as used in Section 355, is ambiguous. It is a well-known maxim of statutory interpretation that when "the terms of a statute [are] unambiguous, judicial inquiry is complete, except in rare and exceptional circumstances." *See Rubin v. United States*, 449 U.S. 424, 430 (1981). Thus, in the absence of any "exceptional circumstances," ambiguities, or indications to the contrary, the court determines that the Federal Circuit's interpretation of the word "claims" in Section 156--an interpretation based entirely on plain meaning--is compelling authority in this court's interpretation of Section 355. *Hoechst* suggests that Bristol's `365 patent claims neither the approved drug (BuSpar®) nor a method of administering it.

In response to this *Hoechst*-based argument, Bristol argues that, unlike the patent at issue in *Hoechst*, its `365 patent is not limited to the use of a metabolite. *See* Bristol Opp'n at 26. Rather, Bristol states that the `365 patent "encompasses a method of use of BuSpar®–*i.e.*, the `oral administration of a precursor or product form of ... buspirone.'" *Id.* (citing `365 patent, Col. 12, lines 3-5). As Mylan correctly points out, however, the prosecution history of the `365 patent shows that: (1) Bristol tried to claim the administration of buspirone as a prodrug; (b) the PTO would

not allow it; and (3) Bristol surrendered that subject matter. *See* Pl.'s Reply at 15. These three facts suggest that just as the patent in *Hoechst* was limited to the metabolite, so too is the `365 patent limited to the use of the metabolite BMY 28674, and therefore the `365 patent cannot claim the administration of buspirone.

Nevertheless, to determine whether Mylan's arguments indicate a substantial likelihood of success on the merits, the court must undertake a preliminary construction of the `365 patent claim. The court must also determine whether the filing of the `365 patent met the second statutory listing requirement of the Hatch-Waxman Act--that is, whether a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of BuSpar®.

**b. The `365 Patent Is Not One "With Respect to Which a Claim of Patent Infringement Could Reasonably Be Asserted"**

A statutory prerequisite to Orange Book listing is that "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the [approved] drug." *See* 21 U.S.C. § 355(c)(2). For the purposes of a preliminary injunction, Mylan makes two arguments that suggest that Bristol cannot satisfy this statutory prerequisite. First, Mylan argues that during the prosecution of the `365 patent prosecution, Bristol expressly surrendered the subject matter it now contends is covered by the claim of the `365 patent--the administration of buspirone. *See* Mot. for Prelim. Inj. at 7 n.4, 25-27. Second, Mylan argues that even assuming that the claim of the `365 patent covers the administration of buspirone, it cannot cover the

administration of buspirone as currently approved by the FDA. *See* Pl.'s Reply at 13.

To determine whether Mylan's arguments are correct--and whether the `365 patent is one with respect to which a claim of patent infringement could reasonably be asserted--the court must determine the proper construction of that claim.

**(1) Claim Construction--The `365 Patent Expressly Disclaims Coverage of the Administration of Buspirone in the Manner Currently Approved**

The construction of a patent claim is a matter of law exclusively for the court. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976-78 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). "It is well settled that, in interpreting an asserted claim, the court should look first to the intrinsic evidence of record, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "Such intrinsic evidence is the most significant source of the legally operative meaning of the disputed claim language." *Id.* (internal quotation marks omitted)). By contrast, the court should look to the extrinsic evidence only if the intrinsic evidence alone fails to resolve any ambiguity in a disputed claim term.

Even within the intrinsic evidence, "there is a hierarchy of analytical tools." *See Digital Biometrics, Inc. v. Identix, Inc.*, 149 F.3d 1335, 1344 (Fed. Cir. 1998). "The actual words of the claim are the controlling focus." *Id.* (citing *Thermalloy, Inc. v. Aavid Eng'g, Inc.*, 121 F.3d 691, 693

(Fed. Cir. 1997)). "The written description is considered, in particular to determine if the patentee acted as his own lexicographer, as our law permits, and ascribed a certain meaning to those claim terms. If not, an ordinary meaning, to one skilled in the art, of the claim controls." *Id.*; *see also Vitronics Corp.*, 90 F.3d at 1582 ("Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or the file history"). In construing the words of the claim, "the specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." *Vitronics Corp.*, 90 F.3d at 1582. Indeed, the specification is considered "the single best guide to the meaning of a disputed term." *Id.*

Turning to the first tool in claim construction--the actual words--the court observes that the `365 patent contains a single claim:

> A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of [BMY 28674] or a pharmaceutically acceptable acid addition salt, or hydrate thereof.

Mot. for Prelim. Inj. at 21 (citing `365 patent, col. 16, lines 26-32). In construing this claim, it is necessary to determine what "systemic administration of an effective but non-toxic anxiolytic dose" of BMY 28674 means.

Mylan and Bristol agree that the rules of claim construction require the court to construe the phrase "systemic administration" in view of the disclosure in the

specification of the `365 patent. *See* Bristol Opp'n at 24 (citing *Vitronics Corp.*, 90 F.3d at 1582); Mot. for Prelim. Inj. at 21 (same). Here the specification states that:

> Systemic administration of BMY28674 may be accomplished by oral administration of a precursor or prodrug form of BMY28674, *e.g.*, buspirone, to mammals.

Mot. for Prelim. Inj. at 21-22 (citing `365 patent, col. 12, lines 3-8). According to Bristol, the specification teaches that there are at least two ways systemically to administer 6-hydroxy-buspirone to treat anxiety. *See* Bristol Opp'n at 24-25. The first way is direct administration of 6-hydroxy-buspirone, referred to in the patent as BMY 28674. *See id.* at 25. The second way, says Bristol, is oral administration of a prodrug such as buspirone. *See id.* Indeed, the specification itself speaks of both direct administration of BMY28674 and oral administration of a prodrug. *See id.* In light of the rules of claim construction, Bristol argues that the phrase "systemic administration" in claim 1 of the `365 patent must be construed as it is expressly defined in the patent itself, *i.e.*, as embracing direct administration and oral administration. Thus, Bristol concludes, unlike the patent at issue in *Hoechst*, the `365 patent is not limited to use of a metabolite. Rather, it encompasses a method of use of BuSpar®–*i.e.*, "the oral administration of a precursor or prodrug form of BMY 28674, *e.g.* buspirone." *See* Bristol Opp'n at 26 (citing `365 patent, Col. 12, lines 3-5).

To be properly filed with the FDA and listed in the Orange Book, the `365 patent must cover the same method of

using BuSpar® as is currently approved.[15] The flaw in Bristol's argument is that it does not address the fact that the `365 patent expressly disclaims coverage of the administration of buspirone in the manner currently approved. For example, the specification states:

> However, this method of systemic administration of BMY28674 improves upon and *differs from the known standard method of oral administration of buspirone.*

Mot. for Prelim. Inj. at 21-22 (citing `365 patent, col. 12, lines 3-8) (emphasis added). The specification also states that the claimed invention "is in contradiction to currently-accepted methods of administration" and "is directly counter to the past method of orally administering buspirone." *See* Pl.'s Reply at 13 (citing `365 Patent, col. 12, lines 17-18, 58-59).[16]

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[15] In determining whether a claim of patent infringement can reasonably be asserted against one who manufactures, uses or sells BuSpar®, one looks only to currently approved uses of buspirone. *See* Pl.'s Reply at 13 n. 12; FDA Opp'n at 28 (the "FDA requires NDA sponsors to submit to the agency for listing only patents covering approved uses of the drug or uses for which the NDA applicant is seeking approval")

[16] During oral argument, Mylan offered the following analogy to explain why Bristol made these representations in the patent specification:

> Let's assume that a Bristol scientist had found ... that a particular chemical compound in an apple was metabolized in the human body into a compound we will call "Apple-A" and that when you administer Apple-A it improve[s] health.... They file a patent application and get a patent on the systemic administration of Apple-A.... They make tablets with Apple-A. They sell those tablets. They want to stop other people from making tablets with Apple- A in them. That is fine. That is a complicated case

Mylan explains that these references to "currently accepted methods of administration" and "the past method of orally administering buspirone" are to the currently accepted uses of BuSpar® as reflected in the BuSpar®™ labeling--a labeling that the statute requires Mylan to use with respect to its buspirone product. *See* Mot. for Prelim. Inj. at 19. Thus, Mylan argues, according to the `365 patent itself, the use of BuSpar® in accordance with its current labeling would not infringe the `365 patent.[17] *See id.* For this reason, Mylan interprets the specification to suggest that "the proper construction of the claim of the `365 patent does not cover the conventional mode of administering buspirone--that method set out in the approved NDA for BuSpar®." Mot. for Prelim. Inj. at 22. If Mylan is correct--and Bristol has not suggested why it would not be--the `365 patent cannot claim a method of using BuSpar® (buspirone) with respect to which a claim of patent infringement could reasonably be

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> involving issues of inherency. This is not a complicated case because what they have done here is they have tried to use this patent to stop people from selling and eating apples by arguing that when you eat an apple, it is metabolized in the human body into the equivalent of the Bristol metabolite, the equivalent of Apple-A.

Tr. at 16.

[17] In support of its argument, Mylan cites Bristol's Press Release of November 21, 2000, in which Bristol states: "with this patent protection, the company will undertake additional clinical research and development activities to elucidate the optimal use of BuSpar®, information that may be submitted for potential labeling changes." *See* Mot. for Prelim. Inj. at 19 (citing Leff Decl. Ex. 8). The court agrees with Bristol that the words of the patent itself, not the press release, define the legal scope of the `365 patent. *See* Bristol Opp'n at 25 n.9 (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Accordingly, the court will not rely on Bristol's press release for guidance as to the meaning of the `365 patent claim.

asserted. *See id.* (citing 21 U.S.C. § 355(b)(1)).

Indeed, in its opposition brief, Bristol provides a lengthy and persuasive discussion of why Mylan's Section-viii-Statement argument lacks merit. *See* Bristol Opp'n at 17-22. By contrast, Bristol devotes little attention to Mylan's construction of the claim of the `365 patent. *See* Bristol Opp'n at 25-27. Instead, Bristol dismisses Mylan's points as "intricate arguments of non- infringement and invalidity" and "sophisticated efforts to construe patent claims." Bristol Opp'n at 27. According to Bristol, "all that is necessary to establish that a reasonable claim of infringement could be asserted here" is that "Mylan seeks FDA approval to market generic buspirone to treat anxiety ... and the `365 patent, as discussed above, covers (among other things) the use of buspirone to treat anxiety." *Id.*

In making this argument, Bristol ignores the fact that "the scope of patent claims is as specific and concrete as the boundaries of real property." *See* Pl.'s Reply at 14; *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1274 (Fed. Cir. 1992) ("The Supreme Court has likened patent claims to the description of real property in a deed `which sets the bounds to the grant which it sanctions'") (citing *Motion Picture Patents Co. v. Universal Film Mfg. Co.*, 342 U.S. 502, 510 (1917)). As Mylan notes, "[i]t is no more sufficient to say that the patent `covers the use of buspirone to treat anxiety' than it would be for one to say that his property is defined by the area around the old oak tree at the top of the hill." Pl.'s Reply at 2.

Bristol has not challenged Mylan's construction of the `365 patent claim. Bristol has not rebutted Mylan's arguments that if Bristol tried to extend the coverage of the `365 patent to past methods of administering buspirone, the

patent would be invalid. In short, Bristol has not refuted Mylan's showing that the `365 patent is not one with respect to which a claim of patent infringement could reasonably be asserted.

**(2) Claim Construction--Bristol Surrendered the Claim Coverage of the Administration of Buspirone During the Prosecution of the `365 Patent**

Bristol's argument that the `365 patent is not limited to the use of a metabolite is unconvincing for still another reason: in the prosecution history, Bristol surrendered the subject matter it now says is covered by the claim of the `365 patent, namely, the administration of the prodrug.

The prosecution history of a patent--part of the intrinsic evidence of a patent claim's scope--contains the complete record of all the proceedings before the PTO, including any express representations made by the applicant regarding the scope of the patent claims. *See Vitronics Corp.*, 90 F.3d at 1582. "As such, the record before the [PTO] is often of critical significance in determining the meaning of the claims." *Id.* Moreover, the prosecution history "limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution." *Southwall Tech., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995).

The Federal Circuit has repeatedly held that when a patent applicant surrenders subject matter during the prosecution of the patent, it cannot then assert a claim that encompasses the surrendered subject matter. *See, e.g., Spectrum Int'l v. Sterilite Corp.*, 164 F.3d 1372, 1379 (Fed.

Cir. 1998) ("a patentee, after relinquishing subject matter to distinguish a prior art reference ... `cannot during subsequent litigation escape reliance [by the defendant] upon this unambiguous surrender of subject matter"); *Southwall Tech., Inc.*, 54 F.3d at 1576 ("The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution"); *Zenith Labs. v. Bristol-Myers Squibb*, 19 F.3d 1418, 1421 (Fed. Cir. ("Prosecution history serves as a limit on the scope of claims by excluding any interpretation of the claim language that would permit the patentee to assert a meaning for the claim that was disclaimed or disavowed during prosecution in order to obtain claim allowance"); *see also Alshtrom Machinery, Inc. v. Clement*, 13 F. Supp.2d 45, 48 n.2 (D.D.C. 1998) ("During the claim construction stage, the prosecution history is ... limited to `exclud[ing] any interpretation that was disclaimed during prosecution") (citation omitted), *aff'd sub nom. Kamyr, Inc. v. Clement*, 217 F.3d 860 (Fed. Cir. 1999).

During Bristol's prosecution of an application related to the `365 patent, "the Patent Examiner rejected Bristol's claim covering the administration of buspirone (rather than the metabolite) as anticipated or, in the alternative, obvious over the prior offer for sale and public use of buspirone, *i.e.*, its administration to patients more than one year before the effective filing date of the application." *See* Mot. for Prelim. Inj. at 7 n.4. As Mylan explains, the Patent Office identified two distinct inventions--the use of BMY 28674 and the use of a prodrug of BMY 28674 (*i.e.*, buspirone). *See* Pl.'s Reply at 12. Bristol was then forced by the Patent Office to choose

between these two inventions.[18] *See id.*

Initially, Bristol elected the prodrug subject matter, amending the claim to recite only the use of a prodrug of BMY 28674, but the Patent Office rejected those claims as anticipated by the prior-art use of buspirone to treat anxiety. *See* Pl.'s Reply at 12. In response to this rejection, Bristol chose to prosecute a divisional application directed to the other invention--use of BMY 28674 itself--and again amended the claims, this time to delete reference to a prodrug. *See id.* Bristol then filed a continuation-in-part application adding language to the specification distinguishing the invention over the prior art use of buspirone. *See id.* According to Mylan, "it was this narrowed claim that Bristol was finally able to gain allowance of in the `365 patent." *Id.* at 12.

Mylan argues that as a matter of law, Bristol cannot recover the prodrug subject matter surrendered by it as a result of the restriction requirement in the parent application. *See* Pl.'s Reply at 12. The Federal Circuit has spoken to this issue, stating that:

> Common sense dictates that a divisional application filed as a result of a restriction requirement may not contain claims drawn to the invention set forth in the claims elected and prosecuted to patent in the parent application. The divisional application must have claims drawn only to the "other invention."

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[18] Under what is known as a "restriction requirement," a patent claim may contain only a single invention. *See* 35 U.S.C. § 121 (Divisional Applications). "If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions." *Id.*

*Gerber Garment Tech., Inc. v. Lectra Sys., Inc.*, 916 F.2d 683, 687 (Fed. Cir. 1990); *see also Spectrum Int'l*, 164 F.3d at 1379 ("a patentee, after relinquishing subject matter to distinguish a prior art reference ... `cannot during subsequent litigation escape reliance [by the defendant] upon this ambiguous surrender of subject matter"); *Zenith Labs. v. Bristol-Myers Squibb Co.*, 19 F.3d at 1421 ("Prosecution history serves as a limit on the scope of claims by excluding any interpretation of the claim language that would permit the patentee to assert a meaning for the claim that was disclaimed or disavowed during prosecution in order to obtain claim allowance"). Thus, Mylan argues, under *Gerber* and its kin, and the prosecution history, the `365 patent cannot claim the administration of buspirone at all. The court finds this argument persuasive.

In its opposition brief, Bristol makes no attempt to reconcile the prosecution history of the `365 patent with its proffered construction of the `365 patent claim. In fact, only during oral argument did Bristol address this issue, referring the court to a document in the prosecution history, dated July 18, 2000, called "Preliminary Communication to the Examiner." *See* Tr. at 37. According to this document, Bristol explained, "it [was] clear that the term `systemic administration' appearing in the claim presently before the examiner as defined in the specification specifically includes the oral administration of the buspirone pro-drug form of the metabolite even if the general term pro-drug no longer appears in the claim.... the deletion of the term pro-drug from the claim did not change the scope of the applicant's claimed intention." *Id.* What Bristol did not tell the court, however, was that the Preliminary Communication to the Examiner was part of an application that Bristol expressly abandoned.

*See id.* at 60-61.[19] Thus, even at oral argument, Bristol failed to explain why it should not be bound by its surrender of the coverage of the administration of buspirone during the prosecution history.

Accordingly, for the reasons discussed above, and in light of Bristol's failure to rebut many of Mylan's persuasive arguments, the court determines that Mylan has demonstrated a substantial likelihood of success on the merits.

### 2. Whether Mylan Will Suffer Irreparable Harm if the Injunction is Not Granted

Though Mylan has demonstrated a substantial likelihood of success on the merits, it has failed to establish that it will be irreparably harmed if the court does not grant it injunctive relief. This court has held that "to establish irreparable injury justifying preliminary relief, the plaintiffs must show that the injury is certain, great, and actual, not theoretical; injury must be imminent, creating a clear and present need for equitable relief to prevent harm." *Varicon Int'l v. Office of Personnel Mgt.*, 934 F. Supp. 440, 448 (D.D.C. 1996). In addition, Mylan must demonstrate "that the injury [is] more than simply irretrievable; it must also be serious in terms of its effect on the plaintiff." *Gulf Oil Corp. v. Dep't of Energy*, 514 F.Supp. 1019, 1026 (D.D.C. 1981).

Mylan asserts that the FDA's refusal to grant immediate final approval of Mylan's ANDA causes irreparable injury to

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[19] Even if the Preliminary Communication to the Examiner had not been part of an abandoned application, Bristol would still have to explain the fact that it chose to prosecute a divisional application directed to the other invention--use of the metabolite BMY 28674--and amended its claim to delete reference to the prodrug.

Mylan. *See* Mot. for Prelim. Inj. at 34. Specifically, Mylan claims that: (1) "it loses revenues for every day that it could be manufacturing and selling its Buspirone Product," *Id.*; (2) "if the FDA does not accept Mylan's Section viii Statement, Mylan would be forced to file a Paragraph IV certification and may, as a result, lose its 180 day exclusivity which would have a devastating affect [sic] on Mylan's sales," *Id.*; (3) "Mylan has also suffered, and will continue to suffer loss of credibility with its customers as a result of its inability to make promised deliveries," *Id.*, and (4) the inevitable drop in stock prices when earnings fall short of expectations may lead to such irreparable harm as employee layoffs and increased vulnerability to a takeover, *see* Pl.'s Reply at 19.

The D.C. Circuit is hesitant to award injunctive relief based purely on lost opportunities and market share. *See Mylan Pharms., Inc. v. Shalala*, 81 F. Supp.2d 30, 42 (D.D.C. 2000); *Berman v. DePetrillo*, 1997 WL 148638, *2 (D.D.C. 1997) ("the loss of a business opportunity is a purely economic injury, and economic loss alone, however substantial, does not constitute `irreparable harm'"); *see also Barton v. District of Columbia*, ---F. Supp.2d ---, 2001 WL 210102, at *11 (D.D.C. 2001) (Urbina, J.); *Bristol-Myers Squibb Co. v. Shalala*, 923 F.Supp. 212, 221 (D.D.C. 1996) (mere speculation about potential market share does not constitute irreparable injury); *Mead Johnson Pharm. Group v. Bowen*, 655 F.Supp. 53, 56 (D.D.C. 1986) (purported loss of market share was "pure speculation"), *aff'd*, 838 F.2d 1332 (D.C. Cir. 1988).

It is true that this court has found irreparable harm where the moving party made a "strong showing that economic loss would significantly damage its business above and beyond a simple diminution in profits." *See Mylan*, 81 F. Supp.2d at 42; *Express One Int'l, Inc. v. United States Postal*

*Serv.*, 814 F.Supp. 87, 91 (D.D.C. 1992) (bidder demonstrated irreparable injury where loss of ten-year $1 billion contract would cause annual loss of $130 million, would impair bidder's relationships with subcontractors and would likely cause capital costs and layoffs); *McGregor Printing Corp. v. Kemp*, 1992 WL 118794, *5 (D.D.C. 1992) ("the irretrievable monetary loss ... in combination with the loss in employment to [plaintiff's] employees" amounted to irreparable harm).

In this case, Mylan has not shown that its economic losses would be either "irretrievable" or "would significantly damage its business above and beyond a simple diminution in profits." Mylan claims that it faces a potential loss of $31,250,000 during the next year, or about 13 percent of its projected net earnings for the fiscal year ending March 31, 2001. See Pl.'s Reply at 18-19. Mylan does not face the same harm that the plaintiff in *Bracco Diagnostics, Inc. v. Shalala*, 963 F.Supp. 20 (D.D.C. 1997) would have encountered, where the court found that research and development costs incurred by drug manufacturers were significant in light of the company's small size. *See id.* at 28-29. By contrast, as this court recently observed, "Mylan is the nation's largest generic drug manufacturer, with annual sales of approximately three-quarters of a billion dollars." *Mylan*, 81 F. Supp.2d at 43.[20]

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[20] Of course, as this court has noted, "these authorities do not stand for the proposition that a generic drug maker never suffers irreparable harm as a result of having one of its products wrongfully kept off the market." *Mylan*, 81 F. Supp.2d at 43. The D.C. Circuit has recognized that generic drug makers "face continued harm [when they are] denied access to the market." *Id.* (citing *Teva Pharms. USA, Inc. v. FDA*, 182 F.3d 1003, 1011 n.8 (D.C. Cir. 1999) (citation omitted)). "The FDA itself has acknowledged that "[e]very day after the tentative approval during which the subsequent applicant can not market its

Mylan also alleges several forms of non-economic injury. Specifically, Mylan alleges that as a result of the drop in stock prices, which inevitably occurs "when earnings fall short of expectations," Mylan will likely suffer "such irreparable harm as employee layoffs or increased vulnerability to a takeover." *See* Pl.'s Reply at 19. Mylan also claims it will suffer a loss of credibility among its customers as a result of its inability to make promised deliveries. *See* Mot. for Prelim. Inj. at 35. Finally, Mylan argues that if the injunction is not granted, it will lose the 180-day period of market exclusivity to which it claims it is entitled for being the first generic producer for this particular product. Since Mylan fails to support these assertions with specific citations to the record, however, its allegations do not rise above the level of mere speculation.

Accordingly, the court determines that Mylan will not suffer irreparable harm if the requested injunction is not granted.

### 3. Whether the FDA or Bristol-Myers Will Be Injured by the Granting of the Injunction

Any injury to Mylan "must be weighed against ... the extent to which an injunction will substantially injure [another] party." *Serono Labs. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C. Cir. 1998). The FDA argues that it will be harmed by a "disruption of its processes for listing patents and resolving disputes related to listed patents if a

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product represents a lost opportunity both for the subsequent applicant and the consumer." *Id.* (citing *180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 64 Fed. Reg. 42,873, 42,878 (1999)).

preliminary injunction is entered." FDA Opp'n at 35. The FDA is correct, but only to a point. Were this court to order the FDA to accept Mylan's Section viii Statement, ANDA holders could disrupt the process for listing patents by unilaterally deciding the scope of a patent, and then imposing their decisions on the FDA. On the other hand, Mylan is likely to prevail on its contention that Bristol improperly submitted its '365 patent to the FDA for listing in the Orange Book. The FDA has already given tentative approval to Mylan's ANDA. If the court allows Mylan's generic buspirone product to assume its rightful place on the market, and not on the loading dock where it currently sits, this order would not frustrate the FDA's mission to protect the public by ensuring that drugs are safe and effective.

Bristol argues that the requested injunction would cause it substantial harm by denying it a period of exclusivity of up to thirty months. *See* Bristol Opp'n at 31. Since Bristol has not shown that it was entitled to this additional period of exclusivity, however, it cannot show that it would be substantially harmed by competition from generic drug makers.

The likely harm to the defendants, then, does not weigh heavily against preliminary injunctive relief. The court therefore concludes that this factor tilts toward the plaintiff.

#### 4. Prong 4: Whether the Public Interest Favors Granting a Preliminary Injunction

The fourth and final part of the preliminary-injunction analysis instructs the court to consider whether the public interest favors the granting of an injunction. The public interest here is multi-faceted: (1) promoting public access to generic buspirone and (2) promoting industry incentives to

research and develop new drug treatments. *See Mylan Pharm., Inc. v. Henney*, 94 F. Supp.2d 36, 59 (D.D.C. 2000) (Urbina, J.). This duality is embodied in the Hatch-Waxman Act itself, which strives to induce name-brand pharmaceutical firms to develop new drug products while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market. Thus, Mylan is only partially correct when it says the legislative goal of the Hatch- Waxman Act is to "make available more low cost generic drugs." *See* Mot. for Prelim. Inj. at 36 (citing H.R. Rep. No. 98-857, pt. 1, 98th Cong., 2d Sess., at 14 (1984)); *see also* Bristol Opp'n at 32-33 ("the legislative goals of the Hatch-Waxman Act ... are not one-sided").

On the other hand, the public interest does not favor a distortion of the principles of the Hatch-Waxman Act. By creating new--and probably impermissible--ways to extend its monopoly, Bristol not only limits the public's access to low-cost drugs, but impedes the very innovation that Hatch-Waxman is designed to promote.

Accordingly, the court determines that the public interest favors the granting of a preliminary injunction to Mylan.

**D. Motion for Preliminary Injunction Granted**

Mylan has demonstrated a substantial likelihood of success on the merits, possibly the most important factor for preliminary injunctive relief in this Circuit. *See Davenport v. Int'l Bhd. of Teamsters*, 166 F.3d 356, 367 (D.C. Cir. 1999) (absent a showing of likely success on the merits, "it would take a very strong showing with respect to the other preliminary injunction factors to turn the tide in [the plaintiff's] favor") (citation omitted). Specifically, Mylan has

shown a substantial likelihood that this court will issue a declaratory judgment stating that Bristol improperly submitted the `365 patent for listing in the Orange Book. Although Mylan failed to demonstrate that it would suffer irreparable harm, Mylan has demonstrated that the public interest favors granting the injunction, and that the balance of harms to the parties does not weigh against granting the injunction. Accordingly, since Mylan makes such a strong showing on three of the four preliminary-injunction factors, the court concludes that Mylan has met the stringent standard for obtaining a mandatory preliminary injunction.

## VI. CONCLUSION

For the foregoing reasons, the court orders as follows:

Defendant Bristol-Myers Squibb Co. is hereby enjoined to request that Defendant FDA delist U.S. Patent No. 6,150,365 from its publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (also known as the "Orange Book"), that is, Bristol is directed to request the FDA to remove its `365 patent from the Orange Book; and

Defendant Tommy G. Thompson, the United States Food and Drug Administration, and their agents, servants and employees are hereby ordered to grant immediate approval of Mylan's abbreviated new drug application (ANDA) No. 75-272 to market its pharmaceutical product containing buspirone hydrochloride as a generic version of BuSpar®.

An Order directing the parties in a manner consistent with this Memorandum Opinion is separately and contemporaneously executed this 14th day of March 2001.

Ridardo M. Urbina
United States District Judge

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

01-1257

MYLAN PHARMACEUTICALS, INC.

Plaintiff-Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services, BERNARD A. SCHWETZ, D.V.M., Ph.D., Acting Principal Deputy Commissioner, U.S. Food and Drug Administration, and U.S. FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

v.

BRISTOL-MYERS SQUIBB COMPANY,

Defendant-Appellant.

Before MAYER, Chief Judge, NEWMAN and MICHEL, Circuit Judges.

ORDER

Mylan Pharmaceuticals, Inc., files a motion to stay the mandate pending a petition for writ of certiorari.

Upon consideration thereof,

IT IS ORDERED THAT:

The motion is denied.

January 25, 2002 FOR THE COURT

Jan Horbaly, Clerk

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

01-1257

MYLAN PHARMACEUTICALS, INC.,

Plaintiff-Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services, BERNARD A. SCHWETZ, D.V.M., Ph.D., Acting Principal Deputy Commissioner, U.S. Food and Drug Administration, and U.S. FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

v.

BRISTOL-MYERS SQUIBB COMPANY,

Defendant-Appellant.

ORDER

A combined petition for panel rehearing and for rehearing en banc having been filed by the APPELLEE, and a response thereto having been invited by the court and filed by the APPELLANT, and a brief in support of the appellee's combined petition for rehearing having been filed by the Gray Panthers Project Fund, amicus curiae, with leave of the court, and the petition for rehearing and amicus brief having been referred to the panel that heard the appeal, and

thereafter the petition for rehearing en banc and response and amicus brief having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for panel rehearing be, and the same hereby is, DENIED, and it is further

ORDERED that the petition for rehearing en banc be, and the same hereby is, DENIED.

The mandate of the court will issue on January 16, 2002.

FOR THE COURT,

Jan Horbaly
Clerk

Dated: January 9, 2002

**21 U.S.C. § 355 - New drugs**

**(a) Necessity of effective approval of application**

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

**(b) Filing application; contents**

**(1)** Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application

**(A)** full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use;

**(B)** a full list of the articles used as components of such drug;

**(C)** a full statement of the composition of such drug;

**(D)** a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

**(E)** such samples of such drug and of the articles used as components thereof as the Secretary may require; and

**(F)** specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration

date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).

**(2)** An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include -

**(A)** a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a

use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section -

**(i)** that such patent information has not been filed,

**(ii)** that such patent has expired,

**(iii)** of the date on which such patent will expire, or

**(iv)** that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

**(B)** if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

**(3)** **(A)** An applicant who makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to -

**(i)** each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

**(ii)** the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

**(B)** The notice referred to in subparagraph (A) shall state that an application has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

**(C)** If an application is amended to include a certification described in paragraph (2)(A)(iv), the notice required by subparagraph (B) shall be given when the amended application is submitted.

**(4)** **(A)** The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 262 of title 42, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

**(B)** The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of title

42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of clinical trials intended to form the primary basis of an effectiveness claim. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

**(C)** Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except -

> **(i)** with the written agreement of the sponsor or applicant; or
>
> **(ii)** pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

**(D)** A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the

director will document the scientific issue involved.

**(E)** The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

**(F)** No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

**(G)** For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 262 of title 42 (including all scientific and medical matters, chemistry, manufacturing, and controls).

**(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order**

**(1)** Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either -

**(A)** approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

**(B)** give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

**(2)** If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file

patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

**(3)** The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined under the following:

> **(A)** If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses, the approval may be made effective immediately.
>
> **(B)** If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).
>
> **(C)** If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under

paragraph (3)(B) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that -

> **(i)** if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision,
>
> **(ii)** if before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or
>
> **(iii)** if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of title 28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of

business.

**(D)** **(i)** if an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

**(ii)** If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in

clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

**(iii)** If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active

ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

**(iv)** If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change

approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. "bioavailability".

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September

24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

**(d) Grounds for refusing application; approval of application; "substantial evidence" defined**

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that

(1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof;

(2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions;

(3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity;

(4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other

information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or

(5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or

(6) the application failed to contain the patent information prescribed by subsection (b) of this section; or

(7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior

to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.

**(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health**

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds

**(1)** that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved;

**(2)** that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or

**(3)** on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use

prescribed, recommended, or suggested in the labeling thereof; or

(4) the patent information prescribed by subsection (c) of this section was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or

(5) that the application contains any untrue statement of a material fact: Provided, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to

assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

**(f) Revocation of order refusing, withdrawing or suspending approval of application**

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

**(g) Service of orders**

Orders of the Secretary issued under this section shall be served

**(1)** in person by any officer or employee of the department designated by the Secretary or

**(2)** by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

**(h) Appeal from order**

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals or the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original

order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

**(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary**

**(1)** The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon -

**(A)** the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

**(B)** the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will

not supply such drug to any other investigator, or to clinics, for administration to human beings; and

**(C)** the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section.

**(2)** Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including -

**(A)** information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

**(B)** adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

**(3)** **(A)** At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a

"clinical hold") if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

**(B)** For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that -

> **(i)** the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or
>
> **(ii)** the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before November 21, 1997).

**(C)** Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible or it is contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

**(j) Abbreviated new drug applications**

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2) (A) An abbreviated application for a new drug shall contain -

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii) (I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same

as that of the listed drug;

**(II)** if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

**(III)** if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

**(iii)** information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed

under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

**(iv)** information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

**(v)** information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

**(vi)** the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

**(vii)** a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the

listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section -

**(I)** that such patent information has not been filed,

**(II)** that such patent has expired,

**(III)** of the date on which such patent will expire, or

**(IV)** that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

**(viii)** if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

**(B)** **(i)** An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give the notice required by

clause (ii) to -

(I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(ii) The notice referred to in clause (i) shall state that an application, which contains data from bioavailability or bioequivalence studies, has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(iii) If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted.

(C) If a person wants to submit an abbreviated

application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds -

**(i)** that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

**(ii)** that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

**(3)** **(A)** The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

**(B)** The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a

meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

**(C)** Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except -

> **(i)** with the written agreement of the sponsor or applicant; or
>
> **(ii)** pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

**(D)** A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue

involved.

**(E)** The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

**(F)** No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

**(G)** For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

**(4)** Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds -

**(A)** the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

**(B)** information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

**(C)** **(i)** if the listed drug has only one active ingredient, information submitted with the

application is insufficient to show that the active ingredient is the same as that of the listed drug;

**(ii)** if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

**(iii)** if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show -

**(I)** that the other active ingredients are the same as the active ingredients of the listed drug, or

**(II)** that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

**(D)** **(i)** if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is

insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

**(ii)** if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

**(E)** if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

**(F)** information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

**(G)** information submitted in the application is insufficient to show that the labeling proposed for

the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

**(H)** information submitted in the application or any other information available to the Secretary shows that

> **(i)** the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or
>
> **(ii)** the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

**(I)** the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e) of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Secretary has

determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

**(J)** the application does not meet any other requirement of paragraph (2)(A); or

**(K)** the application contains an untrue statement of material fact.

**(5)** **(A)** Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

**(B)** The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined under the following:

**(i)** If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

**(ii)** If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

**(iii)** If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is

brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that -

> **(I)** if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,
>
> **(II)** if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, or
>
> **(III)** if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid

or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

**(iv)** If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after -

**(I)** the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

**(II)** the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not

infringed,

whichever is earlier.

**(C)** If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

**(D)** **(i)** If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

**(ii)** If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

**(iii)** If an application submitted under subsection (b) of this section for a drug,

which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

**(iv)** If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

**(v)** If an application (or supplement to an application) submitted under subsection (b)

of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

**(6)** If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended -

**(A)** for the same period as the withdrawal or suspension under subsection (e) of this section or this paragraph, or

**(B)** if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7) (A) (i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public -

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

**(B)** A drug approved for safety and effectiveness under subsection (c) of this section or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

**(C)** If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list -

**(i)** for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (6), or

**(ii)** if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

**(8)** For purposes of this subsection:

**(A)** The term "bioavailability" means the rate and

extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

**(B)** A drug shall be considered to be bioequivalent to a listed drug if -

**(i)** the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

**(ii)** the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

**(9)** The Secretary shall, with respect to each application submitted under this subsection, maintain a record of -

**(A)** the name of the applicant,

**(B)** the name of the drug covered by the application,

**(C)** the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

**(D)** the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

**(k) Records and reports; required information; regulations and orders; access to records**

**(1)** In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar

information received or otherwise obtained by the Secretary.

**(2)** Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

**(l) Public disclosure of safety and effectiveness data**

Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown -

**(1)** if no work is being or will be undertaken to have the application approved,

**(2)** if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

**(3)** if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

**(4)** if the Secretary has determined that such drug is not a new drug, or

**(5)** upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made

effective if such an application had been submitted.

**(m) "Patent" defined**

For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

**(n) Scientific advisory panels**

**(1)** For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

**(2)** The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

**(3)** The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of -

**(A)** members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

**(B)** members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related

professions;

**(C)** a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

**(D)** two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

**(4)** Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest requirement upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member's own scientific work is involved.

**(5)** The Secretary shall, as appropriate, provide education and training to each new panel member

before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

**(6)** Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

**(7)** The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

**(8)** Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the

rationale for the decision.

BRIEF FOR THE FEDERAL GOVERNMENT
DEFENDANTS - APPELLEES

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IN THE UNTIED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

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No. 01-1257

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MYLAN PHARMACEUTICALS, INC.,

Plaintiff - Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services, BERNARD A. SCHWETZ, D.V.M., Ph.D. Acting Principal Deputy Commissioner, U.S. Food and Drug Administration, and U.S. FOOD AND DRUG ADMINISTRATION.

Defendants - Appellees,

v.

BRISTOL - MYERS SQUIBB COMPANY

Defendant - Appellant.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA IN 00-CV-2876,
JUDGE RICARDO M. URBINA

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May 4, 2001

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IN THE UNTIED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

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No. 01-1257

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MYLAN PHARMACEUTICALS, INC.

Plaintiff-Appellee,

v.

TOMMY G. THOMPSON, Secretary of Health and Human Services, BERNARD A. SCHWETZ, D.V.M., Ph.D. Acting Principal Deputy Commissioner, U.S. Food and Drug Administration, and U.S. FOOD AND DRUG ADMINISTRATION.

Defendant-Appellees,

v.

BRISTOL - MYERS SQUIBB COMPANY

Defendant-Appellant.

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APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF COLUMBIA IN 00-CV-2876,
JUDGE RICARDO M. URBINA

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BRIEF FOR THE FEDERAL GOVERNMENT DEFENDANTS-APPELLEES

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## STATEMENT OF RELATED CASES

This case was not previously before this Court. However, the appellant Bristol-Myers Squibb Company (Bristol - Myers) previously sought and obtained a temporary stay pending appeal (Order dated March 16, 2001), which was lifted by Order dated March 27, 2001.

Bristol - Myers has also appealed the same district court decision to the United States Court of Appeals for the D.C. Circuit. The D.C. Circuit has stayed proceedings in that court pending the outcome of proceedings here. See JA 66. Finally, Watson Pharmaceuticals. Inc. v. Schwetz, No. 01-1285 (Fed. Cir., docketed April 10, 2001), is an appeal from a district court decision from the United States District Court for the District of Maryland, involving a virtually irentical issue. The opening brief in that case is presently due approximately June 11, 2001.

## STATEMENT OF SUBJECT MATTER AND APPELLATE JURISDICTION

Plaintiff-appellee Mylan Pharmaceuticals, Inc. (Mylan) invoked the jurisdiction of the district court pursuant inter alia to 28 U.S.C. 1338(a) (providing district courts with subject matter jurisdiction "of any civil action arising under any Act of Congress relating to patents") and 28 U.S.C. 1331, 1361. See, e.g., Joint Appendix (JA) 475-76 , 8. On March 13, 2001 (JA 3, 74 (docket entry 35)), as corrected on March 14, 2001 (JA 54), and clarified on March 15, 2001 (JA 57), the district court issued a preliminary injunction. The opinion is published at ___ F. Supp.2d ____, 2001 WL 273073 (D.D.C. 2001). Bristol-Myers filed a timely notice of appeal on March 15, 2001. JA 74 (docket entry 40). The appellate jurisdiction of this Court is invoked pursuant to 28 U.S.C. 1292(a)(1) and 1295(a)(1).

## STATEMENT OF THE ISSUE

The crux of this declaratory judgment action is Mylan's contention that U.S. Patent No. 6,150,365 ("the '365 Patent") does not claim the approved pioneer drug product, BuSpar®, a drug manufactured by Bristol-Myers used to treat generalized anxiety disorder, or an approved method of using that drug, and that no claim of patent infringement could reasonably be asserted by Bristol-Myers against an unauthorized party engaged in the manufacture, use, or sale of the drug. As a result, Mylan also contends that Bristol-Myers improperly submitted the '365 patent to the federal Food and Drug Administration (FDA) for listing in a publication entitled "Approved Drug Products With Therapeutic Equivalence Evaluations" (commonly referred to as the "Orange Book"). The district court ruled that Mylan's declaratory judgment action was cognizable under the patent laws and that it could therefore entertain Mylan's request for declaratory and injunctive relief. The question that FDA will address is:

Whether the district court correctly determined that it could entertain Mylan's suit for declaratory and injunctive relief because Mylan1s suit presents a cognizable cause of action under the patent laws.

## STATUTORY AND REGULATORY BACKGROUND[1]

At issue in this case are provisions of the Federal Food, Drug, and Cosmetic Act (FDCA) and agency regulations that pertain to approvals of new drug applications (also known as "innovator" or "pioneer" drug applications) and abbreviated new drug applications (also known as ANDAs or generic drug applications). The statutory

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[1] The pertinent statutory and regulatory provisions are found in Addendum A to this brief.

provisions were added to the FDCA through the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Amendments. Pub. L. No. 98-417, 98 Stat. 1585 (1984), codified at 21 U.S.C. 355, 360cc, and 35 U.S.C. 156, 271, 282.

Title I of the Amendments was intended "to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962." H.R. Rep. No. 857 (Part I), 98th Cong., 2d Bess. at 14 (1984), reprinted in 1984 U.S.C.C.A.N. 2647. Title II was intended to provide a new incentive for research and development of pioneer drugs by "restoration of some of the time lost on patent life while the product is awaiting pre-market approval." Id. at 15, 1984 U.S.C.C.A.N. at 2648. The statutory scheme crafted by Congress represents a delicate balancing of these two policy goals. See Tri-Bio Labs. Inc. v. United States, 836 F.2d 135, 139 (3d Cir. 1987), cert. denied, 488 U.S. 818 (1988). See also Eli Lilly and Co. v. Medtronic. Inc., 496 U.S. 661, 15 USPQ2d 1121 (1990); and Bristol-Myers Squibb Company v. Royce Laboratories. Inc., 69 F.3d 1130, 1132, 1133-34, 36 USPQ2d 1641 (Fed. Cir. 1995).

**1. New Drug Applications (NDAs).**

Under the FDCA, pharmaceutical companies seeking to market "pioneer" or "innovator" drugs must first obtain the approval of the FDA by filing a new drug application (NDA). 21 U.S.C. 355(a), (b). In addition to submitting extensive scientific data demonstrating the safety and effectiveness of the drug, an NDA applicant is required to submit information on any patent that claims the drug or the method of using the drug proposed in the NDA and for which a claim of patent infringement could reasonably be asserted against an unauthorized party engaged in the

manufacture, use, or sale of the drug. 21 U.S.C. 355 (b)(1), (c)(2).[2] The patent information must include the patent number and date of expiration. Ibid. FDA has defined by regulation the following types of patents that may be submitted in conjunction with an NDA: drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents. 21 C.F.R. 314.53 (b).[3]

For patents covering the formulation, composition, or method of using a drug, the NDA applicant must also submit a signed declaration stating that the patent covers the formulation, composition, or use of the product described in the pending or approved application. 21 C.F.R. 314.53(c)(2). If a patent is issued after an NDA has been approved, the required patent information must be submitted to FDA within 30 days of the issuance of the patent. 21 U.S.C. 355(c) (2); 21 C.F.R. 314.53(d) (3). FDA is required to publish patent information for approved drugs, and does so in the Orange Book. See 21 U.S.C. 355(b)(1) & (c)(2); Abbott Laboratories v. Novopharm Ltd., 104 F.3d 1305, 1307 n.1, 41 USPQ2d 1535 (Fed. Cir. 1997).

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[2] "Claims" is a term of art grounded in patent law. See discussion in Hoechst-Roussel Pharmaceuticals, Inc. v. Lehman, 109 F.3d 756, 759, 42 USPQ2d 1220 (Fed. Cir. 1997).

[3] The term "drug substance" means an active ingredient of a drug. 21 C.F.R. 314.3(b). The term "drug product" means the finished dosage form, such as a tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other (inactive) ingredients. Ibid. Process patents are not covered by these patent submission provisions and information on such patents may not be submitted to FDA. 21 C.F.R. 314.53 (b) .

## 2. Abbreviated New Drug Applications (ANDAs).[4]

The Hatch-Waxman Amendments permit the submission of abbreviated new drug applications for approval of generic versions of approved drug products. 21 U.S.C. 355(j). Under the abbreviated procedure, an ANDA applicant may rely upon FDA findings of safety and effectiveness for the pioneer drug in obtaining approval of a duplicate generic product. 21 U.S.C. 35S(j) (2). The timing of approval of ANDAs depends in part on patent protections for the pioneer drug. The FDCA requires that an ANDA contain, among other things, a certification for each patent that "claims the listed drug" or the method of the drug's use for which patent information is required to be filed. 21 U.S.C. 355(j)(2)(A)(vii). FDA has defined by regulation the "listed drug" to mean the approved new "drug product." 21 C.F.R. 314.3(b). The certification filed by the generic manufacturer must state one of the following:

(I) that the required patent information relating to such patent has not been filed;

(II) that such patent has expired;

(III) that the patent will expire on a particular date; or

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[4] The relevant statutory and regulatory framework for the ANDA approval process has been described in Eli Lilly, and Co. v. Medtronic. Inc., 496 U.S. at 676-78; Mova Pharmaceutical Corp. v. Shalala, 140 F.3d 1060, 1063-65, 46 USPQ2d 1385 (D.C. Cir. 1998); and Bristol-Myers Squibb Company v. Royce Laboratories. Inc., 69 F.3d at 1131-32, 1135.

(IV) that such patent is invalid or will not be infringed by the drug for which approval is being sought.

If a certification is made by the generic manufacturer under paragraph I or II indicating that patent information pertaining to the drug or its use has not been filed with FDA or the patent has expired, the ANDA may be approved immediately, and the generic drug may be marketed. 21 U.S.C. 355(j)(5)(B)(i). A certification under paragraph III indicates that the ANDA applicant does not intend to market the drug until after the applicable patent expires, and approval of the ANDA may be made effective on the expiration date. 21 U.S.C. 355(j) (5) (B) (ii).

Of particular relevance to this case, a paragraph IV certification requires the ANDA applicant to give notice of the filing of the ANDA to the patent owner and the NDA holder for the listed drug. 21 U.S.C. 355(j)(2)(B). This notice must include a detailed statement of the factual and legal basis for the ANDA applicant's opinion that the patent is not valid or is unenforceable or will not be infringed. 21 U.S.C. 355(j)(2)(B) (iii); 21 C.F.R. 314.95(c)(6). An applicant whose ANDA is pending when additional patents are listed must certify to the new patents, unless the additional patents are submitted more than 30 days after they were issued. 21 C.F.R. 314.94(a)(12)(vi).

Additionally, for a patent that does not claim a use of the drug for which the ANDA applicant is seeking approval, the FDCA requires the ANDA to include a statement (commonly referred to as a "Section viii Statement") that the patent does not claim a use for which the ANDA applicant is seeking approval. 21 U.S.C. 355(j)(2)(A)(viii); 21 C.F.R. 314.94(a)(12)(iii).

The filing of a paragraph IV certification triggers an important process that affects the timing of an ANDA approval. FDA may approve an ANDA with a paragraph IV certification, and the approval may become effective immediately despite the unexpired patent, unless an action for patent infringement is brought against the ANDA applicant within 45 days of the date the patent owner and NDA holder receive notice of the paragraph IV certification. 21 U.S.C. 355(j)(5)(B)(iii); 21 C.F.R. 314.107(f)(2).[5]

The statute also states that "[u]ntil the expiration of forty- five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of Title 28, for a declaratory judgment with respect to the patent." 21 U.S.C. 355(j)(5)(B)(iii). If a patent action is brought by a patent owner or NDA holder before the expiration of the 45-day period, approval of the ANDA will not become effective until at least 30 months from the date that the patent owner and NDA holder received notice, unless a final court decision is reached earlier in the patent case or the patent court otherwise orders a longer or shorter period. 21 U.S.C. 355(j)(5)(B)(iii).

**3. The Listing Of Patents In The Orange Book.**

**a.** In the Orange Book, FDA publishes patent information only for the approved aspects of a drug product. 21 U.S.C. 355(b)(1) & (c)(2); 21 C.F.R. 314.53(e). The agency has successfully defended that practice. See Pfizer v. FDA, 753 F. Supp. 171 (D. Md. 1990) (NDA holders may

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[5] Under 35 U.S.C. 271(e)(2)(A), the filing of a paragraph IV ANDA is itself considered an act of infringement.

submit to FDA for listing only patents covering the approved drug product).[6]

Specifically, patents submitted for an approved drug product must satisfy two separate criteria. The patent (1) must claim the approved drug product or a method of using the approved drug, and (2) must be one with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug product. 21 U.S.C. 355(b)(1) & (c)(2); 21 C.F.R. 314.53(b).

As to the first criterion, unless the drug substance, formulation, or composition patent claims the listed drug, it may not be submitted for listing in the Orange Book. Similarly, a method-of-use patent must claim an approved method of using the approved drug. 21 C.F.R. 314.53(b) and (C).[7] A patent that covers an unapproved method of treating

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[6] There are two parts to the process of submitting and listing patent information. In the first part, an applicant submits its NDA for approval and files information regarding "any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. 355(b)(1). See discussion, supra, Point 1. In the second part, because an applicant may not receive approval for all of the aspects of the drug as described in the original NDA submission, once the NDA is approved, the applicant must amend the patent submission to list only those patents that meet the listing criteria for the approved drug product. 21 C.F.R. 314.53(c)(2)(ii). See also 21 U.S.C. 355(c)(2) (pertaining to the listing of patent information with respect to, for example, patents obtained after an NDA is approved).

[7] Bristol-Myers' contrary assertion (Bristol-Myers Br. at 35-36, 46-47) is incorrect.

an approved indication may not be listed in the Orange Book.[8]

As to the second criterion - that the patent is one "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug" -the drug referred to is the approved drug. The approved drug is that product specifically approved in the NDA as described in 21 C.F.R. 314.50. This is therefore the drug that an ANDA applicant will seek approval to duplicate and for which the patent protections are intended. As the court in Pfizer observed, "[t]here is nothing in the legislative history [of the Hatch-Waxman Amendments] to indicate that Congress intended to provide [the protections of the patent listing process, notice, and 30 month stay] to a product [the sponsor] has chosen not to make available to the American public." Pfizer, 753 F. Supp. at 177. A patent on a new method of using a previously approved drug will only be listed in the Orange Book when that new method of use is approved by FDA, and thus made available to the American public.

**b.** In the event of a dispute as to the accuracy or relevance of patent information submitted to, and subsequently listed by, FDA, an FDA regulation provides an informal process for resolving the dispute. 21 C.F.R.

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[8] The declaration that must be submitted in conjunction with a method-of-use patent for an approved drug reads "The undersigned declares that Patent No. ____ covers the formulation, composition and/or method of use of (name of drug product). This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act * * *." 21 C.F.R. 314.53(c)(2) (emphasis added). The patent, therefore, must claim the approved method of use of the approved drug, in the same way that a submitted patent must claim the approved formulation of the approved drug.

314.53(f). Pursuant to the regulation, an ANDA applicant must provide written notification of the grounds for dispute to FDA. Ibid. Upon receipt of the notification, FDA requests the NDA holder to confirm the correctness of the patent information and listing. Ibid. Unless the patent information is withdrawn or amended by the NDA holder, FDA will not change the patent information listed in the Orange Book. Ibid.

## STATEMENT OF THE CASE

### A. The Factual Background.

Bristol-Myers manufactures the drug buspirone hydrochloride (hereinafter referred to as "buspirone") under the brand name BuSpar®. FDA approved BuSpar@ in 1986. JA 11.[9] In its application for BuSpar®, Bristol-Myers included information on patent 4,182,763 ("the' 763 patent"). Upon approval of the NDA, the '763 patent was listed in the Orange Book for BuSpar®, and was due to expire on May 22, 2000. JA 12. Under the recently enacted pediatric exclusivity provisions of the FDCA, 21 U.S.C. 355a, Bristol-Myers extended its exclusive rights for the sale of buspirone tablets until November 21, 2000. Ibid.

Mylan submitted an ANDA for a generic version of buspirone tablets on December 11, 1997. Mylan's ANDA contained a paragraph III certification to the '763 patent under 21 U.S.C. 355 (j)(2)(A)(vii)(III), stating that it would not market its drug product until the expiration of Bristol-Myers' '763 patent. FDA "tentatively approved" the Mylan ANDA on August 2,2000, making the drug eligible for final

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[9] FDA approved the 5mg and 10mg tablet of BuSpar® on September 29, 1986. The 15 mg tablet of BuSpar® was approved on April 22, 1996.

approval upon the expiration of Bristol-Myers' exclusivity period in November 2000. Ibid. However, on November 21, 2000, the last day of this exclusivity period, Bristol-Myers was issued the '365 patent, and filed information with FDA on the '365 patent that same day. Bristol-Myers stated in its declaration that the patent "is a method of use patent covering, among other things, a method of using BuSpar® for all of its approved indications." As a result of FDA's receipt of the '365 patent and declaration, Mylan's buspirone product was not eligible for approval on November 22, 2000, and the agency did not give final approval to Mylan's ANDA (or to any other ANDAs for generic buspirone tablets) at that time. JA 12-13.[10]

Shortly after Bristol-Myers submitted the '365 patent to FDA, the agency received from Mylan, as well as Danbury Pharmacal, Inc. (Danbury), another firm with a pending ANDA for buspirone, copies of a press release issued by Bristol-Myers on November 21, 2000, regarding the '365 patent. As described in the press release, the '365 patent covers "a method of use of a metabolite produced by the administration of [buspirone.]" JA 13-14.[11]

Following its submission of the Bristol-Myers press release, Mylan submitted to FDA, by letter dated November 22, 2000, what it characterized as a "Section viii Statement" under 21 U.S.C. 355(j) (2) (A) (viii), in which Mylan asserted that the labeling of its drug in the ANDA did not include the method-of-use claimed by the '365 patent.

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[10] On March 28, 2001, pursuant to the district court's preliminary injunction in this case, FDA gave final approval to Mylan's ANDA for generic buspirone tablets.

[11] A "metabolite" is a new molecule that is created after an existing pharmaceutical agent breaks down in the body. JA 13 n.6.

Subsequently, in correspondence dated November 24 and 27,2000, Danbury argued to FDA that, under this Court's ruling in Hoechst-Roussel Pharmaceuticals. Inc. v. Lehman, 109 F.3d 756, 42 USPQ2d 1220 (Fed. Cir. 1997), a patent for a metabolite could not "claim a listed drug" within the meaning of the FDCA. JA 14.[12]

In light of these submissions, and faced with apparently contradictory information about the '365 patent, FDA requested additional input. Specifically, because the Bristol-Myers press release appeared to suggest that the '365 patent was for a metabolite of buspirone, and a decision by this Court suggested that patents for metabolites do not "claim" the listed drug, FDA requested clarification from Bristol-Myers as to whether the patent claimed only a metabolite of buspirone, or the drug itself. JA 14-15.

By letter, FDA therefore asked Bristol-Myers to submit "a declaration that the '365 patent issued by the [Patent and Trademark Office] on November 21, 2000, contains a claim for an approved use of buspirone hydrochloride [the approved drug] that is separate from the claim for 6-hydroxy-buspirone [the metabolite] described in the November 21, 2000, Bristol-Myers Squibb press release." JA 15. FDA explained that, if the sole claim in the '365 patent were for the use of a metabolite of buspirone, FDA might not be able to list the patent in the Orange Book in view of this Court's analysis in Hoechst-Roussel. JA 453-55.

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[12] In Hoechst-Roussel, this Court:: examined patent extension provisions of the Hatch-Waxman Amendments that were passed simultaneously with the provisions governing patent listing and generic drug approvals. These patent extension provisions are administered by the United States Patent and Trademark Office. This Court concluded that a patent on a metabolite, or a method of using a metabolite, does not "claim" a drug product in which the parent drug is the active ingredient. Hoechst-Roussel, 109 F.3d at 759.

In such an event, Mylan's ANDA could then have been approved by FDA, allowing Mylan to market its generic product.

FDA also sent separate letters to Mylan and Danbury explaining its course of action and inviting each company, and any other interested party, to submit additional legal analysis to help FDA determine the impact of this Court's opinion on the patent listing process. Rather than submitting the requested legal analyses, however, and before FDA had received clarification from Bristol- Myers, both Mylan and Danbury filed suits in different federal courts. Mylan filed the instant suit on November 30, 2000, naming both FDA (and its officials) and Bristol-Myers as defendants. Danbury filed suit in the District of Maryland the same day, naming then-FDA Commissioner Henney as the sole defendant. Both actions sought preliminary injunctive relief to prevent the listing of the '365 patent and require FDA to immediately approve the buspirone ANDAs. JA 15.

Shortly after the filing of these lawsuits, Bristol-Myers submitted to FDA the declaration requested in the agency's November 30, 2000 letter. JA 15-16. In its accompanying letter to FDA, Bristol-Myers reiterated that "the '365 patent does not simply claim a method of using [the metabolite], but also claims a method of using [buspirone itself]." JA 16 (brackets in original).

Based on Bristol-Myers' submission, and consistent with its long-standing administrative practice of accepting at face value the accuracy of such patent declarations, FDA concluded that this Court's ruling in Hoechst-Roussel was inapplicable to the matter before it because the '365 patent did not solely claim a metabolite. Ibid. Accordingly, FDA notified Bristol-Myers that the information it had submitted adequately responded to the agency's concerns, and that the

'365 patent would therefore be deemed to have been listed in the Orange Book on November 21, 2000. Ibid. This action meant that Mylan's ANDA for its generic version of buspirone could not be approved at that time.

**B. Statement of the Legal Proceedings to Date.**

1. Mylan filed this action on November 30, 2000. JA 71 (docket entry 1); JA 448. On March 13, 2001, the district court granted Mylan's motion for a preliminary injunction. JA 1, 3, 74 (docket entry 34).[13] Addressing subject matter jurisdiction first, the district court ruled that, in seeking to have the Bristol- Myers' '365 patent "de-listed," Mylan was not trying to enforce the FDCA but, rather, was prosecuting an independent action with respect to a patent pursuant to 28 U.S.C. 1338(a) (providing district courts with subject matter jurisdiction "of any civil action arising under any Act of Congress relating to patents"). JA 19-20, 27-29.

Turning to the factors for granting a preliminary injunction, the court then found that Mylan had demonstrated a likelihood of success on the merits of its patent claim, namely that Mylan had demonstrated a strong likelihood that Bristol-Myers' '365 patent did not claim the buspirone product for which Bristol-Myers had earlier obtained FDA approval and that no claim of patent infringement could reasonably be asserted by Bristol-Myers against an unauthorized party engaged in the manufacture, use, or sale of the drug. JA 31-33. Specifically, the court found that the '365 patent does not claim a method of using BuSpar® (JA 33-37), that the '365 patent expressly disclaims coverage of the administration of buspirone in the manner currently approved (JA 37-43), and that during the prosecution of the

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[13] The order was corrected on March 14, 2001 (JA 54) and clarified on March 15, 2001 (JA 57).

'365 patent, Bristol-Myers had surrendered the coverage of the administration of buspirone at issue in Mylan's ANDA (JA 43-47).

The court next found that Mylan failed to establish that it would suffer irreparable injury (JA 47-50), but that the balance of harms to the parties tilted in favor of Mylan (JA 50-51), and that the public interest weighed in favor of granting a preliminary injunction (JA 51-52). On balance, even though Mylan had not demonstrated irreparable injury, the district court granted a preliminary injunction largely because Mylan had demonstrated a strong likelihood of success on the merits of the claim that the '365 patent did not claim the buspirone product for which Bristol- Myers had obtained FDA approval and that the '365 patent is not one with respect to which a claim of patent infringement could reasonably be asserted. JA 52-53. The preliminary injunction ordered Bristol-Myers to immediately "de-list" – i.e., take the appropriate steps to remove -the '365 patent from the Orange Book, and ordered FDA, upon receipt of Bristol-Myers' request that the '365 .patent be "de-listed," to immediately approve Mylan's ANDA. JA 1, 53, 57. The court also required Mylan to post a $25 million bond as a condition precedent to the "de-listing." JA 58. Thus, the district court's order meant that Mylan could begin marketing its generic version as soon as it posted the bond and Bristol-Myers requested "de-listing."

2. Bristol-Myers appealed to both the D.C. Circuit and this Court. JA 74 (docket entries 40 and 41). This Court issued a temporary stay of the district court's order on March 16, 2001 (JA 59), but dissolved the stay on March 27, 2001 (JA 61), and set the appeal for expedited briefing (JA 64). The D.C. Circuit stayed proceedings in 'that court pending the outcome of proceedings here. JA 66.

## STANDARD OF REVIEW

Whether the district court correctly determined that Mylan's suit for declaratory and injunctive relief was cognizable under the patent laws is a purely legal issue. Accordingly, it is subject to de novo review. See, e.g., DuPont Merck Pharmaceutical Co. v. Bristol-Myers Squibb Co., 62 F.3d 1397, 1401, 35 USPQ2d 1718, 1722 (Fed. Cir. 1995).

## SUMMARY OF ARGUMENT

1. FDA will address only the question of whether the district court correctly determined that Mylan's suit for declaratory and injunctive relief was immediately cognizable under the patent laws. FDA believes that the district court's ruling was correct. FDA will not address whether the district court, having determined that it could entertain the suit, properly exercised its discretion in granting a preliminary injunction. That issue depends in substantial part on whether Mylan demonstrated a likelihood of success on the merits and that issue, in turn, involves a question of patent law - namely, whether the '365 patent claims BuSpar® or an approved use of that product -as to which FDA has no expertise. As we demonstrate in this brief, FDA has only a ministerial duty in listing patents in the Orange Book, and therefore is not authorized to resolve disputes about the validity, accuracy, or relevancy of specific patents submitted to it for listing by pioneer drug manufacturers. Accordingly, all patent disputes regarding the ANDA approval process are to be resolved in private patent litigation. For these reasons, FDA cannot and, therefore will not, express any opinion on the merits of the patent issue presented in this case.

Moreover, because the instant patent dispute should be resolved in private patent litigation, FDA will also not

address the other preliminary injunction factors -irreparable injury, balance of harms, and the public interest.

2. a. As stated above, the underlying merits issue in this case is whether the '365 patent claims BuSpar® or an approved use of that product and with respect to which a claim of patent infringement could reasonably be asserted. If not, as Mylan asserts, Bristol-Myers improperly submitted the '365 patent to FDA for listing in the Orange Book. FDA, however, plays only a ministerial role in the listing of patent information in the Orange Book. Therefore, Mylan's claim that Bristol-Myers improperly submitted the '365 patent for listing in the Orange Book does not state a cause of action against FDA. Instead, Mylan must seek relief against Bristol-Myers. Moreover, because the FDCA restricts enforcement of the FDCA to suits by the United States, see 21 U.S.C. 337(a), Mylan's cause of action against Bristol-Myers cannot arise under the FDCA.

b. In FDA's view, Mylan has a cognizable cause of action against Bristol-Myers for "de-listing" under the patent laws. Using as a guide the "well-pleaded complaint rule" for analyzing a purported declaratory judgment, the Court does not look to the declaratory judgment complaint to determine which federal law is the basis for the declaratory judgment action but, rather, to the action that the declaratory defendant would have brought. With respect to the ANDA approval process, the hypothetical suit that Bristol-Myers would file is a patent infringement suit under 35 U.S.C. 271(e)(2)(A) in response to Mylan's hypothetical filing of a paragraph IV ANDA (because the filing of a paragraph IV ANDA constitutes an act of infringement under section 271(e)(2)(A)). In response to Bristol-Myers' hypothetical patent infringement suit under 35 U.S.C. 271(e)(2)(A), Mylan would have been able to defend, inter alia, on the ground that it should not have had to file a paragraph IV

ANDA in the first instance because the '365 patent did not claim BuSpar® or an approved method of using BuSpar® and that, accordingly, Bristol-Myers improperly submitted the '365 patent for listing in the Orange Book. Therefore, Mylan's declaratory judgment cause of action for that relief is cognizable because it derives from Bristol-Myers' patent law cause of action.

c. Bristol-Myers contends that, even if Mylan could bring a declaratory judgment action for "improper listing," Mylan's suit is barred by 21 U.S.C. 355(j)(5)(B)(iii). In Bristol-Myers' view, that provision requires Mylan to have filed a paragraph IV ANDA and then waited for the expiration of the 45-day period described in that provision before filing a declaratory judgment action. But Mylan1s action -a declaratory judgment action based solely on the claim that the '365 patent does not claim BuSpar® or an approved method of using BuSpar® (and is not a patent with respect to which a claim of patent infringement could reasonably be asserted) - falls outside the scope of 21 U.S.C. 355(j)(5)(B)(iii). This is so because 21 U.S.C. 355(j)(5)(B)(iii) bars only declaratory judgment actions that raise the same allegations that an ANDA applicant is required to raise in the context of a paragraph IV certification. The certification in a paragraph IV ANDA. alleges that a listed patent is invalid, unenforceable, or will not be infringed by the proposed generic product, but does not allege the kind of claim that Mylan is making here (i.e., that the listed patent does not claim the approved product or method of using that product and is not one with respect to which a claim of patent infringement could reasonably be asserted) -which is the sole allegation of Mylan's declaratory judgment action. Hence, Mylan's declaratory judgment action, which does not advance an allegation required to be made in a paragraph IV ANDA, falls outside the bar of 21 U.S.C. 355 (j)(5)(B)(iii) .

**d.** In sum, the type of declaratory judgment action not barred by 21 U.S.C. 355(j)(5)(B)(iii) is extremely narrow. It focuses on the condition precedent to filing a paragraph IV ANDA, namely whether the patent listed in the Orange Book claims the listed drug product or a method of using that product and with respect to which a claim of patent infringement could reasonably be asserted against an unauthorized party. However, it cannot raise the issue of whether the patent is invalid, unenforceable, or will not be infringed by the generic drug product, all of which must be raised via the paragraph IV certification procedure.

## ARGUMENT

### The District Court Correctly Determined That Mylan's Suit Presented A Cognizable Cause Of Action Against Bristol-Myers Under The Patent Laws.

The only issue FDA will address is whether the district court correctly determined that Mylan's suit for declaratory and injunctive relief was immediately cognizable under the patent laws. As we now demonstrate, this aspect of the district court IS decision was correct.

### A. FDA Plays Only A Ministerial Role In Listing Patent Information In The Orange Book, So Mylan's Cause Of Action For "De-Listing" Is Against Bristol-Myers, Not FDA.

**1.** The underlying merits issue in this case is whether the '365 patent claims BuSpar® or an approved method of using BuSpar®, and with respect to which a claim of patent infringement could reasonably be asserted by Bristol-Myers against an unauthorized party engaged in the

manufacture, use, or sale of the drug. If not, as Mylan contends, then Bristol-Myers improperly submitted the '365 patent to FDA for listing in the Orange Book.

Under the FDCA, however, FDA is not authorized to resolve disputes about the validity, accuracy, or relevancy of specific patents submitted to it. See 21 U.S.C. 355(b) (1) ("the [FDA] shall publish [the patent] information" submitted to it by the pioneer drug manufacturer in connection with a new drug application, if the application is approved) (emphasis added). See also 21 U.S.C. 355(c)(2) (if the pioneer drug manufacturer was unable to file the patent information with the original application, because, for example, "the patent was issued after the [new drug] application was approved," it must file such patent information "not later than thirty days after the patent involved is issued," and "[u]pon submission of [this] patent information * * *, [FDA] shall publish it.") (emphasis added). In short, FDA plays only a ministerial role in the listing process. See Abbott Laboratories v. Novopharm Ltd., 104 F.3d at 1307 n.1 (" [t]he FDA must accept as true the patent information supplied by the patentee, such as the patent expiration date"). See also Ben Venue Laboratories. Inc. v. Novartis Pharmaceutical Corp., 10 F. Supp.2d 446, 456, 49 USPQ2d 1920 (D.N.J. 1998).

Consistent with its ministerial obligations, FDA has implemented the patent-listing provisions by informing interested parties what patent information is to be submitted, who must submit the information, and when and where to submit the information. See 21 C.F.R. 314.53(a), (b), (c), and (d). FDA does not scrutinize the substance of the declarations provided by pioneer manufacturers in connection with listing patent information so long as all of the required information has been submitted. 21 C.F.R. 314.53; 59 Fed. Reg. 50338, 50345 (1994). Indeed, FDA has

consistently maintained that it has neither the resources nor the expertise to resolve patent issues. See 54 Fed. Reg. 28872, 28910-11 (1989) (preamble to proposed regulations); 59 Fed. Reg. at 50345 (cols. 2, 3) (preamble to final regulations in which FDA rejected two comments that asserted that "FDA should ensure that patent information submitted to the agency is complete and applies to a particular NDA"). See also id. at 50342-43, 50349, 50352.

In addition, FDA has established a limited process for correcting patent information errors. See 21 C.F.R. 314.53(f). Under 21 C.F.R. 314.53(f), interested parties can dispute the accuracy or relevance of the patent information, and FDA will follow up with an inquiry to the pioneer drug company. See discussion, supra, at p. 11. However, as with the original submission of patent information and consistent with its ministerial role in listing patents, FDA does not scrutinize the pioneer's responses to the follow-up inquiry. 21 C.F.R. 314.53(f). Thus, unless the pioneer drug company withdraws or amends its patent information, FDA will not change the patent information in the list. Ibid. See also 59 Fed. Reg. at 50345. Thus, pursuant to the regulation, if the applicant wishes to pursue the ANDA approval process, the applicant must submit a certification to the contested patent. The regulation does not purport to prohibit an ANDA applicant from pursuing a patent listing challenge -as described, infra, in Point B(2) -in a narrowly-framed declaratory judgment action outside of the paragraph IV certification procedure. If an ANDA applicant pursues such a patent listing challenge, the ANDA is not eligible for approval by FDA while the patent at issue remains listed in the Orange Book.[14]

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[14] In promulgating 21 C.F.R. 314.53 (f), FDA noted that, "[i] f there is no change to the patent information in the list, a section 505(b) (2) or 505(j) [21 U.S.C. 355(b)(2) or 355(j)] application submitted for the drug must, despite any disagreement, contain a certification for each

In light of this statutory and regulatory framework, g11 patent disputes arising out of the ANDA approval process are to be resolved in private patent litigation, not by FDA. See, e.g., 21 U.S.C. 355(j)(5)(B)(iii) (if ANDA applicant believes a listed patent will not be infringed by the ANDA applicant's generic drug product or that the patent is invalid or unenforceable, ANDA applicant must file a certification to that effect with its ANDA, must give notice to the pioneer drug manufacturer of its certification, and cannot receive immediate approval of its ANDA if, within 45 days of the notice, it is sued for patent infringement by the pioneer drug manufacturer). Consequently, Mylan can seek relief for "de-listing" only against Bristol-Myers, not FDA.

### B. Mylan Has A Cause Of Action Against Bristol-Myers, But It Is Under The Patent Laws, Not The FDCA.

#### 1. Mylan does not have a cause of action against Bristol-Myers under the FDCA.

The FDCA restricts enforcement of the statute to suits by the United States. See 21 U.S.C. 337(a) ("Except as provided in subsection (b) of this section [regarding suits by states in their own names], all such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States."). Thus, "[i]t is well settled * * * that the FDCA creates no private right of

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listed patent and any patent challenge must then be pursued through private legal action under the patent laws." 54 Fed. Reg. at 28910 (col. 3) (emphasis added). See also 59 Fed. Reg. at 50345 (col. 3) (as a general matter, FDA "expressly required an applicant to make 'an appropriate certification for each listed patent,' notwithstanding any disagreement as to the correctness of the listed patent information"). These comments indicate that, consistent with our discussion in the text, any continuing dispute over the propriety of a patent listing must be resolved through private patent litigation.

action." In re: Orthopedic Bone Screw Products Liability Litigation, 193 F.3d 781, 788 (3d Cir. 1999), citing 21 U.S.C. 337(a). See also PDK Labs., Inc. v. Friedlander, 103 F.3d 1105, 1113, 41 USPQ2d 1338 (2d Cir. 1997) (holding that plaintiff's suit "represents an impermissible attempt to enforce the FDCA through a private cause of action for violations of the FDCA"); Mylan Labs., Inc. v. Matkari, 7 F.3d 1130, 1139 (4th Cir. 1993) (same); Bailey v. Johnson, 48 F.3d 965, 966-68 (6th Cir. 1995); Eli Lilly & Co. v. Roussel Corp., 23 F. Supp.2d 460, 476 (D.N.J. 1998) ("Every federal court that has addressed the issue has held that the FDCA does not create a private right of action to enforce or restrain violations of its provisions and accompanying regulations."). And see Buckman Company v. Plaintiffs' Legal Committee, 121 S. Ct. 1012, 1017, 1018 n.4, 1019 (2001). Mylan, therefore, does not have a cause of action against Bristol-Myers for "de-listing" under the FDCA and, in fact, did not pursue such a cause of action. See JA 19 (Mylan "does not seek to enforce the [FDCA] against Bristol").

**2. Mylan's cause of action against Bristol-Myers is under the patent laws.**

As the district court found, Mylan's cause of action against Bristol-Myers is under the patent laws. Using as a guide the "well-pleaded complaint rule" for analyzing a purported declaratory judgment, this Court does not look to the declaratory judgment complaint to determine which federal law is the basis of the declaratory plaintiff's cause of action (and whether federal court jurisdiction exists) "but to the action that the declaratory defendant would have brought." See Speedco, Inc. v. Estes, 853 F.2d 909, 912, 7 USPQ2d 1637 (Fed. Cir. 1988). See also Fina Oil and Chemical Co. v. Ewen, 123 F.3d 1466, 1470, 43 USPQ2d 1935 (Fed. Cir. 1997) ("We apply [the well-pleaded complaint rule] not to the declaratory judgment complaint

but to the hypothetical action the declaratory defendant would have brought.").[15]

As the discussion below demonstrates, Mylan's claim that the '365 patent does not claim BuSpar® or an approved method of using BuSpar® (and is not a patent with respect to which a claim of patent infringement could reasonably be asserted) -and that Bristol-Myers therefore improperly submitted the '365 patent to FDA 1527 for listing in the Orange Book -arises under the patent laws. Hence, the district court had subject matter jurisdiction to entertain Mylan's declaratory judgment action under 28 U.S.C. 1338(a), and Mylan's cause of action was cognizable without having to follow the procedures established in 21 U.S.C. 355 (j)(5)(B)(iii) .

**a**. The critical provision is 35 U.S.C. 271(e)(2)(A), which states that "[i]t shall be an act of infringement to submit * * * an [ANDA] application [under the FDCA] * * * for a drug claimed in a patent or the use of which is claimed in a patent * * * if the purpose of such submission is to

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[15] Speedco and Fina Oil used the "well-pleaded complaint rule" to determine whether the district court in those cases had subject matter jurisdiction to entertain the suits at issue. Nevertheless, the principles of the rule serve as a proper guide for determining which federal law is the basis of the declaratory plaintiff's hypothetical cause of action. See Skelly Oil Co. v. Phillips Petroleum Co., 339 U.S. 667, 672 (1950) ("Not every question of federal law emerging in a suit is proof that a federal law is the basis of the suit.") (internal quotation marks and citation omitted). See also Cedars-Sinai Med. Center v. Watkins, 11 F.3d 1573, 1578, 29 USPQ2d 1188, 1192 (Fed. Cir. 1993) ("After constructing a hypothetical complaint that otherwise would have been filed by the declaratory judgment defendant, this court's jurisdictional onus is then to determine both under which federal statute(s) the hypothetical cause of action would have 'aris[en],' and whether those federal statute(s) 'relat[e] to' patents") (citation omitted; brackets in original). The district court here reached the right result though it framed the issue as one of subject matter jurisdiction when it probably should have framed it in terms of a cause of action. WLF's contention (WLF Br. at 16-23) that the district court's discussion of subject matter jurisdiction is a "red herring" is, therefore, of no help to its argument.

obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent." This provision stands as an exception to the broader principle, set forth in 35 U.S.C. 271(e)(1), that it is generally not an act of infringement to take actions "reasonably related to the development and submission of information under a federal law which regulates the manufacture, use, or sale of drugs * * *."

Section 271(e)(2)(A), therefore, creates a "highly artificial" cause of action "for patent infringement in which the mere submission of a paragraph IV certification with an ANDA is deemed the act of infringement. Eli Lilly and Co. v. Medtronic, Inc., 496 U.S. at 678. See also Bristol-Myers Squibb Co., 69 F.3d at 1135. The threshold inquiry in any patent litigation based on the filing of an ANDA is thus whether the ANDA pertains to a drug "claimed in a patent" or to a use that is "claimed in a patent." In keeping with the overall scheme of the Hatch-Waxman Amendments, this criterion parallels those applicable to whether a patent is properly listed in the Orange Book. Sec 21 U.S.C. 355(b)(1) and (c)(2); 21 C.F.R. 314.53(b). Courts have interpreted this parallel structure as requiring that a patent be listed in the Orange Book before an infringement suit can be brought under Section 271(e)(2)(A). See Bristol-Myers Squibb Co., 69 F.3d at 1131-32; Abbott Labs. v. Zenith Labs., Inc., 35 USPQ2d 1161, 1167-69 (N.D. Ill. 1995). Therefore, when Mylan seeks "de-listing" of the '365 patent, it seeks the protection of section 271(e) (1) and asserts that an infringement suit under 271(e)(2)(A) is improper.

Accordingly, assuming arguendo that Mylan had filed a paragraph IV ANDA with respect to the 1365 patent, the hypothetical suit Bristol-Myers would have filed in response to Mylan's paragraph IV ANDA would have been a patent infringement suit based on 35 U.S.C. 271(e)(2)(A). But in a patent infringement suit premised solely on 35 U.S.C. 271(e)(2)(A), one of Mylan's available defenses is that it was not required to file a paragraph IV ANDA in the first instance -because, for example, the '365 patent does not

claim BuSpar® or an approved method of using BuSpar® and that no claim of patent infringement could reasonably be asserted with respect to the patent (and, therefore, that Bristol-Myers improperly submitted the 1365 patent for listing in the Orange Book[16]). Or, Mylan could raise the issue as a counterclaim.[17]

This defense (or counterclaim) is an appropriate response to the section 271(e)(2)(A) patent infringement suit because the filing of a paragraph IV ANDA is conditioned on the existence of a patent that :both "claims the [listed] drug" or "a method of using such drug for which the [ANDA] applicant is seek approval" (and with respect to which a claim of patent infringement could reasonably be asserted against an unauthorized party), and is listed in the Orange Book. 21 U.S.C. 355(j)(2)(A)(vii) .[18] See Lilly and Co. v. Medtronic. Inc., 496 U.S. at 677-78.

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[16] A patent also might be improperly listed because it has expired. See, e.g., Abbott Laboratories v. Novopharm Ltd., 104 F.3d at 1309.

[17] See Abbott Laboratories v. Novopharm Ltd., 104 F.3d at 1309 (affirming district court decision allowing ANDA applicants to counterclaim for removal of patent information from Orange Book in a patent infringement suit brought by pioneer manufacturer); Ben Venue Laboratories. Inc. v. Novartis Pharmaceutical Corp., 10 F. Supp.2d at 452 n.4, citing Abbott Laboratories v. Novopharm Ltd. ("a challenge .to the appropriateness of an Orange Book listing may be raised as a counterclaim in a patent infringement suit").

[18] ee also 21 U.S.C. 355(b)(1) and (c)(2) (directing a pioneer manufacturer to submit patent information for listing in the Orange Book only with respect to a patent that "claims the [listed] drug" or "a method of using such drug"). There is no cause of action for infringement under 35 U.S.C. 271(e) (2)(A) if a patent is not listed in the Orange Book because, if the patent has not been listed, a paragraph IV ANDA is not the proper certification. See 21 U.S.C. 355(j)(2)(A) (vii) and subsection (I). See also Abbott Labs. v. Zenith Labs.. Inc., 35 USPQ2d at 1167-69.

Thus, using the principles of the "well-pleaded complaint rule," see Speedco. Inc. v. Estes, 853 F.2d at 912, Mylan's declaratory judgment action here arises under 35 U.S.C. 271(e)(2)(A). Or, using Bristol-Myers' formulation (Bristol-Myers Br.. at 24), Mylan's declaratory judgment action is the "mirror image" or "inverse" of a suit by Bristol-Myers for infringement under 35 U.S.C. 271(e)(2)(A), not - as Bristol-Myers contends (Bristol-Myers Br. at 24) -a hypothetical suit by Bristol-Myers to declare the '365 patent properly listed.

**b.** Amicus curiae WLF appears to argue that a defense or counterclaim in a patent infringement suit - whether a suit under 35 U.S.C. 271(e)(2)(A) or other patent law provision - is prohibited if the defense or counterclaim seeks relief in the form of "de-listing" (i.e., challenging the NDA holder's listing of the patent in the Orange Book). See WLF Br. at 7 n.8, 12, 13-14. In WLF's view, such a defense or counterclaim seeks to enforce the listing requirements of the FDCA and, therefore, does not arise under the patent laws. Ibid. But, as we just demonstrated, Mylan's cause of action is the contention that the '365 patent does not claim the listed drug, and that contention does arise under the patent laws because it would be a defense to a patent infringement suit filed under 35 U.S.C. 271(e)(2)(A).

Moreover, this Court has already addressed the argument. In Abbott Laboratories v. Novopharm Ltd., 104 F.3d at 1309, the Court held that a counterclaim for "de-listing" was proper in a patent infringement suit. See also n.17, supra. The Court obviously saw "de-listing" as properly arising under the patent laws inasmuch as it was a direct response in that case to a patent infringement suit where the generic manufacturer claimed that the challenged patent had expired and therefore should not be listed in the Orange Book. And Bristol-Myers agrees that a counterclaim for "de-listing" is proper in an appropriately-filed patent infringement suit -for example, a patent infringement suit claiming infringement under 35 U.S.C. 271(e)(2)(A). See Bristol-Myers Br. at 56.

c. Bristol-Myers contends that, even if *it* were otherwise possible for Mylan to assert a claim for "improper listing," Mylan's suit is barred by 21 U.S.C. 355(j)(5)(B) (iii) which, according to Bristol-Myers, bars all declaratory judgment actions by an ANDA applicant unless the applicant has first filed a paragraph IV ANDA and then waited for the expiration of the 45-day period described in 21 U.S.C. 355(j) (5)(B)(iii). See Bristol-Myers Br. at 25-27. See also WLF Br. at 13-16., Bristol-Myers misunderstands section 355(j) (5)(B)(iii)'s scope.

21 U.S.C. 355(j)(5)(B)(iii) does not bar all declaratory judgment actions but, rather, only those that would raise the same issues that an ANDA applicant is required to raise *in* a paragraph IV certification. In this regard, section 355(j)(5)(B)(iii) authorizes FDA to immediately approve a paragraph IV ANDA "unless an action is brought for infringement of a patent which is the subject of the certification * * *." The "action" for infringement referred to is the "highly artificial" one brought pursuant to 35 U.S.C. 271(e)(2)(A) in which the act of infringement is the mere submission of a paragraph IV ANDA.

The section 271(e)(2)(A) "action," therefore, counters the allegations in the paragraph IV ANDA that the patent at issue is invalid, unenforceable, or will not be infringed.[19] In stating that "no action may be brought * * * for a declaratory

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[19] See 21 U. S. C. 355(j)(2)(A)(vii)(IV) ("patent is invalid or will not be infringed); 21 C.F.R. 314.107(b)(3) ("patent is invalid, unenforceable, or will not be infringed"). The "unenforceability" of a patent is not specifically found in the FDCA. See, e.g., 21 U.S.C. 355(b) (2)(A)(iv), 355(j)(2)(A)(vii)(IV), and 355(j)(5)(B)(iv)(II) .Howeve.r, the first court to examine unenforceability in the context of § 355 concluded that the phrase "invalid or not infringed" included unenforceable patents. Merck v. Danburv Pharmacal. Inc., 694 F. Supp. 1, 8 USPQ2d 1793 (D. Del. 1988), aff'd 873 F.2d 1418, 10 USPQ2d 1682 (Fed. Cir. 1989). Accordingly, because the "unenforceability" of a pate~t is a recognized reason why a generic drug product would not vJ.olate a patent holder's rights, FDA has included it in its regulations. See 21 C.F.R. 314.107(b)(3). See also 59 Fed. Reg. at 50339.

judgment with respect to the patent," section 355(j)(5)(B)(iii)'s reference to "action" must be read in a manner consistent with its prior references to "action," "an action," or "such an action." See, e.g., Commissioner v. Lundy, 516 U.S. 235, 250 (1996) ("the normal rule of statutory construction [is] that identical words used in different parts of the same act are intended to have the same meaning") (internal quotation marks and citation omitted). See also Hollowav v. United States, 526 U.S. 1, 7 (1999) ("[T]he meaning of statutory language, plain or not, depends on context.").

Therefore, the declaratory judgment "action" barred for days by section 355(j)(5)(B)(iii) is the one that would raise issues statutorily-required to be raised via the paragraph IV certification procedure. In other words, the 45-day bar in section 355(j)(5)(B)(iii) was meant to prevent the circumvention of the paragraph IV certification procedure by the filing of a preemptive declaratory judgment action that would raise the very issues that the statute requires to be raised in a paragraph IV certification. The allegation made here -that the 1365 patent does not claim BuSpar® and, therefore, was improperly submitted for listing in the Orange Book -is not one of the allegations required to be made in a paragraph IV certification and, therefore, does not circumvent the paragraph IV procedure. Accordingly, Mylan's declaratory judgment action falls outside the scope of the bar in 21 U.S.C. 355(j)(5)(B)(iii).[20]

Moreover, by its plain language, section 355(j)(5)(B)(iii) prohibits declaratory judgment actions with respect to the patent only following the ANDA applicant's

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[20] It is important to emphasize that there is absolutely no incentive for ANDA applicants to file frivolous declaratory judgment actions based on the argument made by Mylan here. Such a filing would only lengthen the pioneer manufacturer's monopoly. In this regard, the filing of the declaratory judgment action would delay the filing of a paragraph IV ANDA. In turn, that delay would delay the start of the 45-day waiting period in 21 U.S.C. 355(j)(5)(B)(iii) and thus the start of the 30-month stay of FDA approval that accompanies the filing of a patent infringement suit under 35 U.S.C. 271(e)(2)(A).

filing of a paragraph IV certification. That section states, "[u]ntil the expiration of forty-five days from the date the notice made under paragraph (2) (B) (i) [the paragraph IV certification] is received, no action may be brought under section 2201 of title 28, for a declaratory judgment with respect to the patent." The statute does not bar Mylan's declaratory judgment action brought prior to filing a paragraph IV certification for the sole purpose of challenging the requirement that it file that certification.

In DuPont Merck Pharmaceutical Co. v. Bristol-Myers Squibb, supra, 62 F.3d 1397, this Court recognized an ANDA applicant's right to file a declaratory judgment action raising the issue of whether it must file a paragraph IV certification before it filed that certification. Id. at 1401. In DuPont Merck, before filing a paragraph IV certification for a listed patent, the ANDA applicants sought a declaratory judgment that section 154(c) of the Uruguay Round Agreements Act (URAA) exempted them from the need to file the certification if they wished to market a generic drug during the Delta period (the period between the original expiration date of the patent and the later expiration date resulting from the extension provided by the URAA). Id. at 1400-1402. As in DuPont Merck, this Court should allow Mylan to seek a declaratory judgment that it need not file a paragraph IV certification.

In accordance with the foregoing discussion, there is no merit to Bristol-Myers' contention that allowing the instant suit to proceed will lead to wholesale circumvention of the paragraph IV certification process. See Bristol-Myers Br. at 25-27 & n.7. Nor is there merit to the WLF's contention that allowing Mylan's suit to proceed permits the generic manufacturer to choose the forum that will decide the patent infringement issues that must be raised via a paragraph IV certification. See WLF Br. at 9, 15.

As stated above, the type of declaratory judgment action not barred by 21 U.S.C. 355(j)(5)(B) (iii) is extremely narrow: it focuses on the condition precedent to filing a paragraph IV ANDA, namely whether the patent listed in the Orange Book claims the listed drug product or a method of

using that product (and with respect to which a claim of patent infringement could reasonably be asserted against an unauthorized party), but it cannot raise the ,issue of whether the patent is invalid, unenforceable, or will not be infringed, all of which must be raised via the paragraph IV certification procedure.[21]

**d.** The legislative history of 21 U.S.C. 355(j)(5)(B)(iii), although scant, is consistent with our position that section 355(j)(5)(B)(iii) does not bar Mylan's suit. In explaining section 355(j)(5)(B)(iii), the House Report stated that "[n]o action for declaratory judgment regarding patent infringement can be brought within 45 days allowed for notice of certification of patent invalidity or non-infringement." H.R. Rep. No. 98-857, Part II, 98th Congo 2d Sess., at 16, reprinted in 1984 U.S.C.C.A.N. 2647, 2700 (emphasis added).

The only difference between this wording and our position is that FDA added "unenforceability" to the allegations that can be made in a paragraph IV certification (and FDA added "unenforceability" because that concept was judicially created after the enactment of the Hatch-Waxman Amendments in 1984). See n.19, supra. Otherwise, the legislative history is entirely I consistent with our view that the 45-day bar in section 355(j) (5) (B) (iii) was meant to bar only declaratory judgment actions that raise exactly the same kinds of patent infringement issues that must be raised in the paragraph IV certification procedure.

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As this brief demonstrates, Mylan has a valid cause of action, but only against Bristol-Myers under the patent laws. Hence, Mylan had no basis for making FDA a

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[21] Moreover, "the breathing space" (WLF Br. at 15) provided by the 45-day waiting period in section 355(j)(5)(B)(iii) -which allows the pioneer manufacturer to evaluate allegations made in a paragraph IV ANDA that the patent is invalid, unenforceable, or will not be infringed by the proposed generic drug product -is not affected by a declaratory judgment action charging that the listed patent does not claim the listed product.

defendant in this action. The district court compounded Mylan's mistake by enjoining FDA to immediately approve Mylan's ANDA once Bristol-Myers requested that FDA "de-list" the' 365 patent. See JA 2, 53, 57. The district court apparently thought it needed to provide this relief in order to ensure that Mylan benefitted from the court's injunction requiring Bristol-Myers to request the "de-listing." But final FDA approval of an ANDA is sometimes delayed for reasons other than the existence of a patent. For example, approval might be held up for lack of good manufacturing practices at the sites where Mylan's ANDA drug product is produced. See 21 U.S.C. 355(j)(4)(A).

Therefore, the district court should have limited its decision to ordering Bristol-Myers to request FDA to "de-list" the '365 patent, and it should have presumed that FDA would act appropriately in light of that action. See, e.g. Bowen v. American Hospital Ass'n, 476 U.S. 610, 626-27 (1986) ("presumption of regularity [is] afforded an agency in fulfilling its statutory mandate") (internal quotation marks and citation omitted). In this case, FDA did approve Mylan's ANDA on March 28, 2001, as it was ordered to do by the district court, but it would have done so even without the preliminary injunction because, as it turns out, the only obstacle to final approval was the listing of the 365 patent. That fact, however, does not vitiate the district court's mistake in ordering FDA to immediately approve Mylan's ANDA. Nonetheless, because, in the circumstances of this case, the district court's injunction against FDA is harmless error, FDA has not separately appealed that aspect of the district court's preliminary injunction.

## CONCLUSION

For the foregoing reasons, Mylan's declaratory judgment action presented a cognizable cause of action that permitted the district court to entertain Mylan's request for declaratory and injunctive relief.

Respectfully submitted,
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MAY 2001

# UNITED STATES CONGRESS

August 17, 2001

The Honorable Tommy Thompson
Secretary of Health and Human Services
Washington, D.C. 20201

Dear Mr. Secretary:

We share an interest in seeing that laws governing intellectual property and regulatory review of pharmaceuticals are implemented in an even-handed manner. The American public deserves the benefits of the latest developments in medicine in the form of new drugs, as well as having affordable generic substitutes available at an appropriate time.

In recent months there have been several reports that pioneer drug firms have used provisions of the pharmaceutical patent laws to extend their patent terms in a manner that raises legitimate questions of fairness.

We are writing to urge the Food and Drug Administration's vigilance in making certain that there is no gamesmanship to undermine competitive interest by allowing

late issued patents to be listed in the Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") on the eve of generic competition. We are hopeful you will direct the agency to exercise its discretion as appropriate and reject a mechanical reading of the law in such cases.

We recognize that some new patents may be valid and may somehow be integral to the already marketed product and therefore can arguably be listed despite their late issuance. At the same time, if the agency determines that the relationship between these new patent claims and the existing product are not well-founded and cannot meet a good faith test, there should be appropriate consequences with respect to the Orange Book.

We understand that the FDA is generally reluctant to engage in detailed patent validity inquiries. But nothing in the agency's governing statute, nor in its regulations, precludes it from carefully reviewing an application for an Orange Book listing, or from declining to list a patent whose applicability to an approved drug product that is frivolous or tenuous on its face. Indeed, such steps by the FDA would be consistent with the Agency's obligation to enforce the requirements of the law.

Your agency has the opportunity to review its practice in this area, as it is our understanding that a request may be made to the FDA within the next few weeks by holders of patents purportedly related to the medication Prilosec. If granted, this request could have the practical effect of extending patent protection on Prilosec, the world's best-selling drug, for two-and-a-half additional years. This could result in American consumers and the federal

government unnecessarily spending hundreds of millions of dollars.

The underlying patent for Prilosec, which is used to treat heartburn, is scheduled to expire on October 5, 2001. Until last month, it appeared that generic drug companies would be able to market lower-cost generic versions of Prilosec on the following day. However, on July 17, 2001, a manufacturer of Prilosec obtained two new patents ("the '085 and '086 patents") for Prilosec and publicly stated that it would seek an eleventh-hour listing of these patents in the Orange Book.

We were heartened by the manufacturer's recent announcement that such a listing would not be sought. The economic consequences of such a decision could be enormous. As you may be aware, under the Food, Drug and Cosmetic Act, once a patent has been listed in the Orange Book by the FDA, the patent holder may bring a patent infringement suit against a generic challenger. Such a suit automatically stays the approval of a generic version for 30 months, or until a court decides that the patent is invalid or unenforceable against the generic product, whichever comes first.

Many are reaching the conclusion that the practice of seeking eleventh-hour Orange Book listings in order to forestall the imminent marketing of a generic product can undermine the Hatch-Waxman Act's goal of facilitating the entry of lower-cost generic drugs into the market. The Act also seeks to protect the legitimate intellectual property interest of brand-name companies. Given the substantial investment required to bring a new drug to market, it is only fair that an innovator firm be able to defend the validity of its intellectual property.

With respect to Prilosec, it is our understanding there may be other late-issued patents whose listing is still undecided. We urge that, consistent with the concern we have outlined above, FDA give careful scrutiny to any request it receives that may have the effect of extending the medication's patent. Thank you for your consideration of our views.

Sincerely,

Henry A. Waxman
Member of Congress

Orrin G. Hatch
United States Senator

Edward M. Kennedy
United States Senator

cc: Acting Principal Deputy Commissioner Bernard A. Schwetz, D.V.M., Ph.D.
Federal Trade Commissioner Chairman Timothy J. Muris